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SOME RECENT ADVANCES IN CANCER WORK.[1]

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A VAST amount of observation, experiment and discussion relative to cancer has been carried on during recent years and has been largely contributed to by some of the most brilliantly intellectual and highly trained men and women in the world of medical science.

An enormous mass of experimental and clinical data has accumulated and the conclusions, suggestions, claims and arguments based upon it which have been put forward from time to time, are almost bewildering in their number, variety and real or apparent contradictions. Nevertheless, out of it can be extracted certain definite facts and apparently sound conclusions of the highest practical and clinical importance.

This review will be divided into two sections. In the first section such facts, extracted from recent research, are set out and such conclusions formulated as appear to have the most important bearing upon clinical aspects of the human cancer problem with which we practising members of the medical profession have to deal.

In the second section certain points in diagnosis and prognosis are referred to, the basic principles of cancer therapy discussed in a general way and an attempt made to define recent advances in the treatment of each of several of the more commonly occurring clinical manifestations of malignant disease.

[1] Read at a meeting of the Victorian Branch of the British Medical Association on August 5, 1925.

I.

RECENT RESEARCH FROM THE CLINICAL ASPECT.

Biological Researches.

The preliminary announcements by Gye and Barnard regarding their recent and current researches, if correct, are of such fundamental importance that no review of cancer research can be attempted without some reference to them. For the purposes of this review it has been thought best to assume that the claims put forward will be properly confirmed in due course.

Unfortunately the full text of their publication has not yet been received in Australia and, of course, until that is available no final analysis nor evaluation can be attempted. At the same time the

information which has appeared in the lay press, appears to be authoritative so far as it goes and to go far enough to give one the impression that a very valuable research method has been devised and that important fundamental discoveries relative to the nature and causation of cancer have already been derived from the application of that method. It is not proposed at the present juncture to discuss nor speculate upon the enormous apparent advantages in every phase of cancer research which may accrue from these discoveries, but it does appear necessary to consider how they affect conceptions built upon other earlier researches at least equally reliable and where this necessity arises attempts will be made to meet it.

A great deal of research has been carried out in the past upon transplantable tumours, with a view to determining the special biological peculiarities of cancer cells as compared with normal ones. Amongst other possibilities it was hoped that by such means one or more special characteristics might be detected which could be exploited in the diagnosis, prevention and cure of malignant disease. But it has recently become clear that many of the most obvious characters exhibited by malignant cells studied under such conditions are not really primary characters of those cells at all, but only expressions of reactions occurring between the transplanted malignant cells and the fluids and tissues of their new hosts (homologous immunity reactions). Consequently the method of homoplastic transplantation has fallen into disfavour. The necessity of securing by other means a constant supply of suitable living malignant tissue for study led to the development of two new methods. One of these methods is the experimental induction of cancer by application of different agents and a number of cases have already been brought forward in each of which definite causative relation between a known agent and a particular cancerous condition has been proved to exist. For example, the following may be cited: Production of sarcomata in rats by X rays, production of carcinomata in rabbits by X rays, occurrence of carcinoma of the bladder in man (but not in animals) as a result of inhaling aniline fumes, occurrence of epitheliomata in man amongst paraffin and shale oil workers, occurrence of sarcoma of the cyst wall of *Tænia crassicollis* in the liver (but not in other organs) of a certain strain of rats, production of sarcomata (but not carcinomata) in rats by tar injections, production of carcinoma of the skin (but not of the alimentary mucosa) in mice (but not in rats) by tar applications, association of cancer with chronic arsenical poisoning in man, production of carcinoma of the gall bladder in guinea pigs (but not in rats) as a result of the experimental introduction of gall stones or pebbles.

It should be noted that in all these cases the cancrogenic agents are regarded as chronic irritants, thus bringing remarkable support to the hypothesis first put forward by Virchow, strengthening the view of numerous subsequent clinical observers and indicating the most profitable field of search for other effective agents.

Now one of Gye's conclusions is that all malignant growths are produced as a result of the cooperation of two factors, one of which (the virus) is common to all, while the other (the specific factor) is peculiar to each. If this be so, it would appear that the virus must be ubiquitous and in that sense the less important of the two factors, while the number and variety of specific factors may be enormous and the determination of their nature, origin and *modus operandi* may provide a problem almost identical with that which faced us when we conceived that its solution lay in the identification of all the modes and agents of chronic irritation effective in cancer induction. In other words the genesis of the specific component in Gye's duplex causation may be very colsely related with that factor which has previously been regarded as effective *per se* and studied under the name of "chronic irritation."

Analysis of the list of "spontaneously" occurring and experimentally produced malignant lesions set out above brings to light another feature very important from the clinical point of view. It will be seen that in the majority of cases a strikingly specific relationship exists between the particular irritation acting and the species or even variety or strain of animal upon whose tissues it produces its malignant effect. Consequently it would by no means follow that any new agent proven by experiment to be cancrogenic towards a particular animal would induce similar effects in man.

Further, even within the species, variety or strain individual variation in susceptibility (or resistance) towards known specific cancrogenic agents has been proved. The question of whether such variation is transmissible by inheritance has been adequately investigated only in the case of the mouse. In that animal it has been shown to follow the rule for Mendelian recessive characters. Neither in man nor in any of the remaining animals is there yet a sufficiency of data to enable a decision to be arrived at directly. In the meantime it should not be overlooked that the Mendelian laws relating to heredity are of general biological significance and not limited to any particular species.

Again, in every one of these cases of cancer genesis, experimental or otherwise, a long "latent period" occurs between the effective application of the irritant and the first appearance of the malignant condition. Consequently it would seem that in further clinical research along these lines upon human subjects any possible causative factors should be sought in the remote rather than in the recent history of patients. In some cases, but not in all, a recognizable precancerous condition precedes the truly cancerous. The proof of the occurrence of this latent period throws doubt upon the generally accepted significance of "age."

From these considerations it would appear that at least in some respects a limitation must be placed upon the value of animal researches and a correspondingly increased importance ascribed to the clinical study of cancer in man and the solutions of some of these problems sought for directly in that relatively neglected field.

In an investigation of the conditions under which tar paintings induce carcinomata in mice, Deelman[1] found that the added effect of mechanical trauma during the latent period sometimes precipitated the development of the neoplasm. It is known that normal cells on injury yield a substance which stimulates their undamaged neighbours to a reproductive activity which has for its object repair of the part. The most probable explanation of the phenomenon observed by Deelman is that from the cells injured by the trauma growth-activating substance is liberated which cooperates with the cancrogenic reaction already in train between the tar irritant and other cells of the part. The same explanation will readily be applied to these otherwise puzzling cases met with clinically in which neoplastic proliferation appears to have some causative connexion with simple trauma. Viewed from this angle hypertrophies and benign tumours respectively also appear to be correlated with varying quantities or intensities of activator production. The special appeal of this point of view is that it brings all these processes into harmony and pathological changes are related to commonly occurring physiological phenomena.

Striking evidence of the development within the body of immunity factors directed against tumours arising from its own tissues (autologous immunity) has been obtained by Murray[2] as a result of his experiments and observations upon animals. He found that when susceptible animals were subjected to the action of appropriate irritation over extensive or multiple areas, in the great majority of cases the development of one malignant focus induced a very intense resistance or relative immunity against the development of another similar focus anywhere in the animal. Further, animals already the victims of spontaneous cancer exhibit the same refractory character. A short time after surgical removal of the first malignant focus this resistance is lost and another focus may appear in the site originally irritated or can be induced elsewhere by application of the same or another appropriate irritant.

Very convincing evidence of the occurrence in man of all the phenomena (including those of autologous immunity) observed in connexion with the experimental induction of cancer in animals is contained in Scott's splendid clinical analysis of the occupation dermatoses of the paraffin workers of the Scottish shale oil industry. The extreme rarity of multiple malignant new growths in the same individual is also a matter of every day clinical experience.

It is to be particularly noted that once these malignant new growths have formed, there is no character, biological or microscopical, by which they differ in any degree from spontaneously occurring cancers. Perhaps the special distinction of "spontaneous" cancers is that their causative irritants have not yet been identified.

Murray suggests that by the further pursuit of these studies we may eventually discover a means of detecting this refractory phase and so acquire a method of early diagnosis of occult cancer. It is also hoped that by devising a safe procedure for inducing it we may obtain a rational means of prevention, control or even cure of cancer. There is a possibility that the method of autoinoculation of minced radiated malignant cells as practised at the Middlesex Hospital will provide the procedure desired in the latter case.

These experimental results of Murray and clinical observations of Scott and others, with the conclusions based equally upon them, are of the highest clinical import. They serve to elucidate many puzzles and lend considerable support to the view, independently arrived at by several radio-therapeutists, that the beneficial effects derived from this method of treatment are largely due to the promotion of immunity reactions.

The other method of obtaining constant supplies of suitable material for study is by the cultivation of cells and tissues *in vitro*. This procedure is difficult and tedious, but highly interesting and important results have been obtained from it and much further work is now proceeding in the direction of comparing fundamental physiological processes in normal and cancerous cells respectively. Several peculiarities of the cancer cell have already been revealed, but it appears likely that all of these rest upon the one basic difference expressed by its special proclivity to cell division.

Results of researches conducted by this method at Copenhagen by Albert Fischer[3] seem to provide interesting confirmation of the widely accepted theory of the cell autonomy of malignant neoplasms. This worker found that normal cells cultured *in vitro* appear quite unable to divide when isolated from their fellows, but do so only when they form part of a more or less organized mass of cells and even then division appears to proceed in a more or less systematic fashion in groups of cells simultaneously; whereas under the same conditions isolated malignant cells multiply without difficulty.

Fischer[3] also found that certain sarcomata which he studied *in vitro*, appeared able to prey upon, that is to grow and multiply at the expense of muscle substance added to the culture medium. This observation suggests that a similar process may play some part in the invasion and replacement of normal tissues by cancer cells within the body.

In vitro cultures are also being used in experimental therapeutics to test the effects and modes of action of various therapeutic agents and some very striking results have been obtained. For instance, it has been found that even six to ten times the so-called lethal dose of X rays have in certain cases failed to kill such cultures.

Other studies[4] of cultures of cells *in vitro* have revealed the existence of a growth-activating factor and that malignant cells maintain within themselves a constant supply (proportional to the degree of their malignancy) of a growth-activator, while non-malignant cells only form an activator on undergoing autolysis, so that in the latter case the amount of new tissue produced is related to the magnitude of the original injury, being, of course, proportionate to the amount of growth-activator

yielded by the destroyed cells. These observations made by Drew have been confirmed by Murray, Russell, Cramer and others. There is a great temptation to find some degree of identity between the growth-activators of Drew and the specific factors of Gye. If one could go farther and postulate that chronic irritation produces its effects by inflicting upon normal cells a succession of injuries which eventually lead, in accordance with Ehrlich's hypothesis, to an established overproduction of growth-activator, all these observations begin to harmonize remarkably well. Gye has apparently thrown no light upon the question of the primary origin of the specific factors which he extracted from tumours. Yet this may really be the crux of the problem.

Other researches indicate that the rate of growth and multiplication of malignant cells are increased by the addition of extract of normal tissues. This may at least in part explain the increased activity both in local and in remote foci of malignant disease which has frequently been observed to follow upon surgical procedures.

Studies of cultures of malignant cells have also revealed the production by malignant cells of something which tends to lead to their own destruction unless rapidly removed and the question arises whether the beneficial results of radio-therapy may not in part be due to stimulating the production of this self-destroying factor, increasing its activity or liberating it more freely from the cells. Against this suggestion, however, is the fact that attempts to inhibit the growth of tumours in animals by means of such toxic substances elaborated *in vitro* by similar malignant cells have so far failed. The beneficial effects of radio-therapy are more convincingly ascribed to other processes which will be discussed later.

Physical Researches.

It is not now proposed to discuss any of the physical researches in detail on account of their highly technical nature and the fact that the results obtained find their chief clinical expression in the form of improvements in apparatus and methods employed in the very specialized field of physiotherapy. Many of these researches are the outcome of valuable cooperation between physicists and medical biologists and in these lines of progress medicine owes a great and increasing debt to the science of pure physics.

Detailed analyses of the characters and properties of α, β and γ rays of radium and of the radiant energy emitted by ultraviolet and Röntgen ray apparatus have been made, the absorption qualities of the different metals have been worked out so that screening and filtering requirements can be satisfied by the simplest and most economic means and the absorption phenomena, effects and mode of action in vital tissues of the different types of radiant energy have been examined. The heterogeneous character of both β and γ rays of radium and of the rays emitted by Röntgen ray apparatus has been established and the several components have been separated and analysed, their respective wave lengths determined and the occurrence of differential action upon living tissues for different wave lengths made evident. The necessity for a radical change from the older empirical and haphazard practices which originally obtained in the field of radio-therapy to new and scientific methods with accurate measurements, has been made very clear. Fallacies and defects in the types of apparatus at present used for producing X rays for therapeutic purposes and in the methods and instruments used for determining the character, quality and quantity of their output have been brought to light and improvements designed to overcome these difficulties and defects. Such advances are continuously proceeding and the governing authorities of up-to-date hospitals and institutions where radiotherapy is employed on any considerable scale, recognize the necessity of including within their staffs properly trained physicists who are competent to take technical charge of such plants and apparatus and to make the necessary checks of the measuring instruments employed and assist in further researches.

Perhaps the most important of the advances thus briefly enumerated is the proof of the differential action of the several wave lengths of radiant energy. This has been demonstrated by Russ[5] and others. For example, Russ found that about six times the dose of very soft rays (0.45 — 0.3 Ångström unit) was necessary to produce an erythema when very hard rays (0.168 Ångström unit) were used, whereas in the case of the lethal dose to a selected tumour it was only 2.6 times as great. It is now generally accepted that the special susceptibility of malignant cells to radiation increases as the wave length is shortened. Since the shortest wave lengths derived from the most efficient of modern X ray plants have a value of about 0.06 Ångström unit, while the shortest γ rays from radium are about 0.01 Ångström unit,[6] the great advantages of the latter source are obvious. By the same reasoning the superiority in the treatment of neoplastic conditions of the so-called "deep therapy" X ray plants over those which yield only rays of the longer wave lengths, must be granted. According to one of the greatest authorities of the day an X ray tube to emit rays of a shortness equal to that of the shortest γ rays of radium would require to be energized at a voltage of about 2,000,000, whereas about 250,000 volts is about the present maximum upon which any reliance can be placed.

Considerable progress in X ray therapy may result when it becomes generally recognized that exact measurement and specification of each of the essential components of dosage (wave length, intensity and time) is necessary. Equivalent spark-gap voltages are quite unreliable as a guide to the quality of the rays emitted from the tube. Wave lengths should be measured directly by the X ray spectrometer or indirectly by their absorption curves in, say, copper. Similarly the milliampère meter gives no true measure of the intensity of radiant output and this latter factor should be measured directly by one of the better type of iontoquantimeter, preferably one which is calibrated against a known quantity of radium. Further, to

insure stability in these factors improved plants such as those now being constructed in France and Germany, which give a constant uniform output from the tube, should be adopted.

II.

In this section, for obvious reasons, only views and practices which have been widely accepted or adequately tested will be included.

Note on Diagnosis.

Clinicians are all more or less seized of the importance of the earliest possible diagnosis of malignant condition and there is a just and very general dissatisfaction regarding the relatively late stages at which the great majority of sufferers continue to present themselves. A definite improvement in this respect would almost certainly result from sound propaganda work and probably is unobtainable by any other means. Nevertheless, it must be recognized that in some cases delay takes place through faulty diagnosis. How some of these errors and deficiencies of diagnosis are to be overcome is not yet apparent, but if the needs are constantly emphasized, the required improvements may be more determinedly sought. For example, all will agree that the early diagnosis of carcinoma of the stomach is very unsatisfactory. It was anticipated that the method of fractional gastric analysis would make for great improvement, but this hope appears to be rapidly receding. Again, a very large proportion of carcinomata arising in the prostate have already invaded neighbouring organs or even led to metastases before they give rise to any symptoms. So convinced of this are members of the staff of the Memorial Hospital, New York, that they have suggested that the only prospect of improvement lies in regular examination of all men passing the age of, say, fifty. In the case of carcinoma of the bowel it is usually held that the first indication of malignancy is evidenced by progressively increasing constipation. Many, however, consider that all too frequently the crisis of acute obstruction first brings to light an underlying malignant condition. The suggestion has lately been put forward that in the early stages of the majority of such cases a phase of hyperperistalsis occurs which manifests itself to the patient in the form of a transitory "turmoil" or "flurry" of the bowels usually occurring soon after meals and it is recommended that in clinical examinations inquiry for this symptom should be made. Again in rectal carcinoma it is held that a spurious diarrhœa precedes other evidences of stricture. The desirability of clearly defining the earliest symptoms or signs arising from each of the several malignant conditions cannot be overemphasized and further clinical investigation along these lines is urgently called for. Such data are essential for propaganda purposes.

Note on Prognosis.

As matters at present stand in any given case of malignant disease it can be safely predicted that without appropriate treatment death from the disease will result unless some other fatality intervenes. Consequently prognosis resolves itself into an analysis of the results obtained by the different methods or combinations of methods of treatment in each of the several types of growth met with. In very few malignant conditions are data available which are sufficiently extensive and reliable to serve as a basis for even approximate estimation of the prognostic chances. By far the most reliable statistics as yet brought forward are those of the British Ministry of Health relative to cancer of the breast and its surgical treatment.[7] Analysis of these brings into prominence the intensive effect upon prognosis of at least three factors which are more or less under control, to wit the superiority of a "complete" operative procedure along such lines as those laid down by Sampson Handley, the paramount importance of operating before the axillary glands are involved and the wisdom of regarding both chronic mastitis and all benign tumours of the breast as definitely precancerous and excising the affected breast by the complete operation. Similar analyses of malignant conditions in other sites and organs are urgently required, but will not be available until the practice is established of recording histories in more uniform, detailed and reliable form. Therein lies an opportunity for valuable clinical research.

Radiographic and other means of searching for metastases should be more frequently employed for prognostic purposes. *Post mortem* and clinical data will supply the indications as to where these searches should be made.

Treatment.

From the dawn of medical history until some twenty odd years ago the one principle in the treatment of cancers was the attempt to remove them completely, preferably by the knife. Operative surgery still provides the best available means of treatment in the majority of cases in which the stage of the disease is not too far advanced. Nevertheless, even its most determined advocates will not claim that its results are satisfactory. It is small wonder then that the search for better methods of treatment has been unabating. Within recent years a certain amount of success has attended this search and it is now becoming recognized that there are malignant conditions in which surgical excision, although practicable, is no longer the method of choice, for example lympho-sarcomata, basal-celled carcinomata, carcinomata of the tongue, tonsil, mouth and pharynx, carcinomata of the *cervix uteri*, epitheliomata of the lip and face, some sarcomata of bones.

Certain minor improvements in surgical technique have resulted from the occasional replacement of the scalpel by the cold cautery (electrocoagulation or surgical diathermy), but the general feeling is that the present methods of operative surgery as applied to malignant neoplasms are not susceptible of any radical improvements.

About the beginning of this century it was discovered that X rays and radium exert a somewhat selective effect upon proliferating tissue cells and especially upon tumour cells. Following upon this

discovery a sort of empirical radio-therapy at once came into being. It speaks well for the intrinsic merits of this form of therapy that it has survived at all, for the procedure usually employed has been so variable and so lacking in scientific principles, the dosage and methods of application have been so haphazard that the surprising thing is not that radio-therapy failed so often, but that it ever succeeded. For a while radiation fell into relative disrepute as a means of treating cancer and was restricted to a rather limited sphere. Within that sphere it was generally accepted that radium rays and X rays had identical qualities and actions and differed only in the greater penetrating power of the former. Subsequently physicists, of whom perhaps Rutherford, Russ and Duane have rendered greatest service, made available to medical science exact data of inestimable value relative to the characters and properties of the radioactive substances and of the rays they emit. Armed with this knowledge several distinguished medical scientists, foremost among whom is Regaud, of Paris, have rebuilt the whole science of radium-therapy, relaid its foundations upon the γ ray and worked out the details of treatment for a number of different conditions to which this method is most appropriate. More or less contemporaneously with these developments in γ ray therapy the Erlangen school of X ray therapists by the adoption of apparatus of high voltage yielding rays of much shorter length, attempted to advance X ray therapy in a similar fashion and to bring it into line with or even supersede γ ray therapy. Several factors, the chief of which are the differential biological action of the different wave-lengths and the importance of a greatly increased "time" component of the dose, have militated against the success of these latter efforts.

The advances in radium therapy will now be briefly summarized. Originally relatively large doses (say ten to two hundred milligrammes) were applied in high concentration within single applicators which filtered off varying proportions of β rays. The times of application in such cases were determined largely by the character of the malignant growth. In superficial non-ulcerating foci the dose was limited by the production of skin injuries. In rodent ulcers and other ulcerating malignant tumours this barrier no longer existed and large doses could be given, while in deeper seated tumours the tubes could be buried and allowed to remain long enough to cause direct local necrosis. Employed in such fashion radium acts chiefly as a specialized caustic differing from other chemical and physical caustics in its much greater penetration beyond the surface of contact. From this point of view its outstanding character is its unnecessary expense. Much of this has now been changed. The basis of the specific action of radium upon malignant tissues has been determined and found to belong chiefly to γ rays. Applicators and methods of filtration have been standardized to yield the greatest proportion of such rays, while reducing β rays to negligible proportions and due regard is now paid to the space distribution of the dose and to the great importance of the "time" factor in dosage. In the technical standards of dosage (quantity, filtration, distribution and time) laid down by Regaud the selected unit of quantity of radium is one milligramme (one millicurie, if emanation is used) and the screening is provided by the containing needle which has a total wall thickness of 0.5 millimetre of platinum, which filters off 99.9% of the primary β radiation with only minimum interference with the γ radiation and yields only negligible amounts of soft secondary radiation. The standard practice is to bury the needles and the rule for space distribution of the dose is, as far as practicable, one milligramme needle to each section of malignant tissue having a diameter of one centimetre. It has been shown independently by many investigators that the susceptibility of animal cells in the phase of subdivision is about six times as great as in the resting phase. Consequently an ideal of first importance is that exposure should be sufficiently long to catch all the cells of the growth in the process of division. Exposures are given for periods up to three or four weeks continuously. Superficial and hypertrophic rodent ulcers are unique and only in their case are the β rays of radium still especially employed.

An attempt will now be made to analyse briefly but critically the biological reactions and *modus operandi* by which the favourable changes are brought about in malignant disease as a result of radiation by γ rays. Such a treatment agency to be ideal would require to have a selective action against the tumour cells and at the same time to conserve and to fortify the body's local and general resistance against cancerous disease. There can no longer be any doubt that tumour cells exhibit a specific sensitivity to γ radiation, although the margin in this respect between malignant and normal cells is rarely very great and differs in the different malignant cell-types. They have been classified in the order of their sensitivity by Ewing[8] as follows:

(i.) All basal-celled carcinomata;

(ii.) All lymphoid tumours, particularly lympho-sarcomata;

(iii.) Many tumours related to the lymphoid group, such as endotheliomata of lymphatic glands, endotheliomata of bone and myelomata;

(iv.) Tumours derived from embryonal cells and retaining the embryonal characters;

(v.) Very cellular, rapidly growing tumours of any type even when derived from adult cells;

(vi.) Conversely tumours derived from adult cells and reproducing cells exhibiting "adult" characters such as squamous carcinomata, neuro-sarcomata, osteo-sarcomata and many adenomatous and benign tumours are relatively very resistant.

That a conserving and fortifying effect is exerted upon the surrounding stroma by γ radiation under

the conditions of a proper technique is also beyond dispute and the histological evidences of these changes and processes have been analysed and their significance confirmed by that greatest of authorities upon neoplastic pathology, James Ewing.[9] The favourable general reactions evoked appear to be chiefly those of a special form of immunity (autologous immunity) and no *in vitro* "tests" comparable to those demonstrable by means of precipitins, agglutinins, lysins and the like in the case of heterologous immunity, have been devised nor are they to be anticipated. However, clinical evidence of the apparent promotion of such immunity or resistance factors by radio-therapeutic measures are commonly observed and were long ago commented upon by such acute and experienced radiologists as Knox[10]. There is also confirmatory experimental evidence. According to the technique employed there are three more or less distinctive grades of γ radiation effect, each of which exhibits some degree of both specific and selective action upon the tumour cells and supporting influence upon the natural defence processes.

Grade I. is characterized by growth restraint and slow recession of tumours. In this grade low intensities of radiation are employed over long periods. Very little appeal is made to the specific destructive influence upon tumour cells and the results depend very largely upon local and general immunity and resistance factors. This grade of irradiation frequently yields valuable results when applied to resistant tumours not amenable to more successful treatment by other methods.

Grade II. is specially characterized by autolytic degeneration of the tumour cells. In this grade the intensities and times of irradiation selected are those which give the optimum value to the specific sensitivity of the malignant cells and in it the local resistance factor is also promoted, while the general immunity factor finds its best expression, probably being related with the autolysed malignant cells. It is the ideal type of γ ray therapy, but unfortunately is not always appropriate to the type of malignant growth or to other essential circumstances. The writer has enjoyed the privilege of examining microscopically specimens obtained by Donaldson from his patients at Saint Bartholomew's Hospital of malignant growth undergoing regression as a result of this grade of radiation treatment and also specimens prepared by Woglom, of Columbia University, of malignant tumours undergoing spontaneous regression. The apparent identity of the characters and changes in the two series was very striking.

In Grade III. the dominant feature is caustic destruction. There is little doubt that beyond the area of destruction the reduced intensity of the rays yields a certain amount of the more specific reaction and some promotion of local resistance factors, but this grade of irradiation appears to have the least favourable influence upon the processes of general immunity. It is employed by some radiologists in dealing with very resistant tumours. Others hold that such types of growth should be attacked by considerably lengthening the time factor rather than by increasing the intensity. A probable reason why cachectic subjects rarely respond favourably to irradiation is that the general immunity factor has already been overcome. When harmful results are seen from radiation therapy, these are probably due to over irradiation of the stroma, normal tissues and blood vessels being injured and the local and general protective mechanisms broken down.

The bases of the so-called "deep X ray therapy" of tumours are somewhat similar to those of γ ray therapy, but it suffers from certain disadvantages, chief of which are the less selective action of rays of longer wave lengths and the special conditions of application both as regards distribution and time. The effective processes upon which it must, however, still rely, are growth restraint, slow specific autolytic destruction of malignant cells with associated immunity reactions, reduction of blood supply to the tumour by obliterating endarteritis, focal necrosis of portions of the tumour by anæmic infarction and fibrosis and encapsulation of the tumour. It is now becoming generally recognized that in the vast majority of cases not only is it not practicable to deliver the so-called deep therapy "lethal dose" to tumours *in vivo*, but the attempt to do so is contra-indicated. The view is fast gaining ground that the true basis of favourable reaction to Röntgen ray therapy is by appeal to the local and general resistance factors already enumerated.

No discussion of radio-therapy, however brief, would be sound unless reference were made to the local and general ill-effects which may result from indiscreet employment or defective method. The local and general ill-effects are: Extensive fibrosis which may interfere with the circulation and so with function. Not infrequently cachexia is induced or increased. Prolonged treatment over a wide area, particularly when the abdomen is involved, may cause extensive sclerosis and destruction of lymphoid tissue. Atrophy of essential organs, such as the thyreoid gland, may be induced. Chronic catarrhal enteritis may be caused by intensive irradiation of the abdomen, as also may destruction of its lining epithelium thus facilitating passage of bacteria and toxins into the blood stream. Damage to intervening and adjacent normal organs may occur. Hæmorrhage into or about the tumour may result. Secondary infection of the degenerated tumour mass may take place. Absorption of secondary decomposition products may occur. Destruction of the blood and blood-forming tissues may be induced. Constitution disturbances may be set up.

Knox[11] urges that a good guide to the general systemic effects in radio-therapy is obtained by frequent blood examinations. The risk of inducing any of these unfavourable results is far less in radium therapy than in X ray therapy. Despite these relative disadvantages "deep therapy" has a present place in the treatment of malignant conditions where for one reason or another radium

therapy by an effective technique has not yet been rendered practicable. Chief among such conditions are extensive superficial malignant growths, neoplasms of the thoracic viscera, stomach and bowels and some uterine malignant tumours. Special attention has been given to radio therapy because as a result of investigations made in England, Europe and America, the writer is convinced that by far the best and most hopeful advances of the last few years have been secured in this field.

Another line of progress in cancer therapy is found in greater attention to the general systemic condition; that is the adoption of such measures as alkalinization in cases where the principal factor in cachexia is an acidosis, blood transfusion in very debilitated or cachectic patients and so forth. The simultaneous or successive exhibition of two or more of the several recognized methods of treatment is considered by many to yield the best results in certain types of cases. Preirradiation and post-irradiation of all conditions in which operative surgery is employed seem likely to become an established principle. Investigations made and comparisons instituted by the writer have led to the conviction that the standards of diagnosis and treatment of malignant conditions are definitely higher in specialized institutions, such as the New York Memorial Hospital and the Middlesex Hospital (Cancer Section) than in the leading general hospitals of the same cities.

Analysis of the results being obtained in the principal international centres of cancer work from the employment of the several methods at present available, yields valuable indications for the treatment of several of the more commonly occurring malignant conditions. These indications will now be briefly summarized. Details of technique have not been considered appropriate to the present article.

1. Lymphosarcomata belong exclusively to the field of radio-therapy. They should never be incised even for diagnostic purposes.

2. Embryonal tumours in children should always be radiated. Subsequent operative removal may be desirable.

3. Cutaneous cancers and precancerous conditions, basal celled, should be treated by surface irradiation and squamous celled, by needles. Quiescent pigmented moles should never be irradiated, but widely excised.

4. In epitheliomata of the lip and face surgery yields excellent results during the early stages, but even in these radium accomplishes as much or more without mutilation or risks of dissemination. Small growths should be irradiated from the surface by cross-fire and larger ones by buried needles. Related lymphatic glands should also be irradiated.

5. Squamous carcinomata of the tongue, mouth and tonsil should be dealt with by preliminary surface irradiation followed by buried needles and irradiation of related glands. Very gross lesions may first be reduced by diathermy. Preliminary ligation of the lingual or external carotid arteries may be advisable in some cases. Both Regaud and Ewing consider that practically every such primary tumour should be "cured" by buried radium.

6. Mixed tumours of salivary glands are very amenable to irradiation.

7. Carcinoma of the œsophagus in the cricoid region should be treated by irradiation, elsewhere no method of treatment is very satisfactory, but perhaps radium yields the best palliative results.

8. Treatment of carcinoma of the stomach is very unsatisfactory by any present method. Effective radium technique has not yet been devised. The best prospect for progress probably lies in earlier diagnosis, preliminary irradiation, then complete surgical excision in earliest cases, gastro-enterostomy (when practicable), followed by deep X ray therapy in others.

9. For intestinal carcinoma preliminary irradiation followed by complete excision when practicable, is indicated; otherwise surgical short-circuiting of affected part of the bowel should be carried out, followed by deep X ray therapy.

10. In rectal carcinoma good results are rarely obtained by any method. Quick, of the New York Memorial Hospital, employs radium needles followed by diathermy.

11. In carcinoma of the larynx surgery and radium therapy are about equally favoured at present. In Paris the "radium collar" is in great favour.

12. For uterine cervix cancer radium therapy by short, massive, concentrated doses is employed at Radiumhemmet, Stockholm and the New York Memorial Hospital and by prolonged irradiation with small divided doses from the surface (in Paris) and by buried needles (by Donaldson at Saint Bartholomew's Hospital, London). The last method appears the best and should be supplemented by deep therapy irradiation of the iliac glands. Subsequent hysterectomy should not be performed. Rarely extensive fungating masses may be first removed by diathermy.

14. For uterine corpus cancer radium, sometimes followed by hysterectomy, may be employed. Deep X ray therapy may supplement radium therapy in cases of extensive pelvic involvement.

15. For mammary carcinoma preliminary irradiation of the breast and the surrounding area by "hard" X rays and of axillary glands by radium should be followed when practicable by "complete" surgical excision with postoperative burial of radium in the region of the supraclavicular and parasternal glands and subsequent systematic post-operative "prophylactic" surface irradiation. Inoperable cases are treated by a combination of radium needles buried in the tumour and lymphatic glands and hard X rays applied externally. Operation prior to involvement of the axillary glands is of paramount importance. All breasts with chronic mastitis or benign tumours should be regarded as at least precancerous and should be excised by the complete operation.

16. Of malignant tumours of bone, some round-celled sarcomata are very amenable to treatment by radium. Surgical results upon osteogenic sarcomata are very bad and usually involve crippling

of the patient. Buried radium, with external hard X ray therapy, has arrested some and should be tried more extensively.

17. For brain and spinal cord tumours external irradiation is usually employed, but more should be treated by exposure and insertion of radium needles, as investigations have proved the high resistance to irradiation of normal brain and cord tissue.

18. For carcinoma of the prostate radium needles should be buried through the perineum or by cystostomy incision, supplemented by radium tubes in urethra and rectum. Radiograms of the pelvis and lumbar spines should always be taken, as metastases here are so early and so frequent.

19. For carcinoma of the bladder radium needles should be buried through the suprapubic incision. Precancerous papillomata may be treated by diathermy or radium.

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DIABETES.[1]

By EUSTACE RUSSELL, M.B., Ch.B. (Edinburgh),
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I WOULD like first of all to express to you my appreciation of the compliment you pay me in asking me to address you at this meeting. I have chosen *diabetes mellitus* as the subject for tonight partly because I have had some opportunity of studying the treatment of the disease at the Brisbane Hospital and partly because I think some practitioners have a very erroneous impression as to the use of "Insulin" in the treatment of the disease.

There are, of course, two distinct methods of treating *diabetes mellitus*, one with "Insulin" and the other without it and it is perfectly certain that the man who is not familiar with the treatment of diabetes without "Insulin," is a positive danger to the patient whom he attempts to treat with it.

Let me say that the further I go, the less I make use of "Insulin" and I think that there has been a considerable abuse of this valuable remedy by those who have not understood the principles of treatment of the diabetic.

I would like briefly to refer to the work of Banting to whose zeal and enthusiasm we are indebted for the wonderful discovery of "Insulin" in the first place. It was first suggested to Banting that it was possible to get an active extract of the islets of Langerhans tissue, from the observation that on ligation of the ducts it is the acinous tissue which degenerates and not the islet substance; this was investigated in the dog.

It was found that a filtrate of the gland macerated in Ringer's solution would reduce the blood sugar of a partly depancreatized dog and it was found that the injection of the solution exercised a definite influence not only on the blood sugar, but on the sugar excreted in the urine. Various sources of "Insulin" were tried, including the pancreas of the fœtal calf and eventually it was discovered that the pancreas of the ox could be used and the preparation became a clinical possibility.

It was found that given by the rectum the preparation was inert and by the mouth almost so, but given intravenously or subcutaneously the blood sugar was reduced rapidly enough and for a period of time.

The original unit of "Insulin" was the amount required to reduce the blood sugar of a rabbit weighing a kilogram to 0.045% or to produce convulsions. The value of the unit has been altered twice, because originally it was found that the rabbit unit was too potent and this was reduced by one third and this has again been altered.

Next in importance to Banting's discovery and indeed the basis of all diabetic treatment are the experiments of Allen who showed that a dog partially depancreatized could be kept alive and in fair health by the restriction of the diet, whereas a dog which was partially depancreatized and fed to the full, developed glycosuria and rapidly died. This underfeeding is the fundamental principle of practically all diabetic treatment and should be known and understood. Briefly put it aims at keeping the patient thin and fit rather than fat and sick.

In regard to the diagnosis of diabetes it can be said at once that there is no royal road to the diagnosis. It is often enough discovered by accident, perhaps in the majority of instances, and this emphasizes the absolute necessity for the routine examination of the urine with great care of every patient seen either in the consulting room or on the daily round and for preference the examination of a mixed twenty-four hour specimen or a specimen passed, say, half an hour after a meal.

As to the type of individual who developes diabetes, it may be mentioned that all alcoholics are on the diabetes black list and all "pot bellies" are candidates in the race for the disease, so that their urine should be made the object of even more careful and punctilious examination.

There is apparently an hereditary or familial tendency to the disease and all close relatives should

[1] Read at a meeting of the Ipswich Medical Society on July 18, 1925.

be watched for the signs of the complaint. The blood sugar examination is the real test in the diagnosis of *diabetes mellitus* and the glucose tolerance of the individual is the most certain guide to the making of a certain diagnosis.

It has been shown that the blood sugar of a normal individual is about 0.1% and that after the ingestion of a certain quantity of glucose the percentage of sugar in the blood rises rapidly to about 0.16% or so and then falls to normal in about one and a half hours. Sugar does not pass into the urine in a normal individual until the blood sugar concentration reaches 0.18% and it can be said *en passant* that it is quite a difficult matter to cause glycosuria in the normal subject.

In the diabetic a different state of affairs obtains. The blood sugar content is high in diabetes, in a fasting diabetic 0.21% is about the average and it is possible to judge the severity of a case from the blood sugar concentration, anything above 0.24% being put in the category of severe.

In the glucose tolerance test in the diabetic there is a slow return to the normal and the blood sugar concentration is often higher hours after the experiment than it was when the experiment began.

There is a type of glycosuria known as renal glycosuria in which there is an absence of the signs and symptoms of diabetes, albeit there is plenty of sugar in the urine and there is also a low blood sugar concentration. It would appear that there is in these cases a low renal threshold and that the sugar passes into the urine at a much lower concentration level than that obtaining in the normal subject. It is advisable to note that there are certain diseases and abnormal states of health in which there is an increase in the percentage of the blood sugar; these have to be borne in mind to guard against the possibility of error.

In cases of arterial hypertension, nephritis, myxœdema, hyperthyreoidism, acromegaly, pregnancy and diseases of the liver there is apt to be a state of hyperglycæmia and after the administration of certain drugs and thyreoid extract the same state of affairs sometimes occurs.

As to the height to which the blood sugar concentration may advance, there are cases on record in which the blood sugar was 1.40% and even more, but these cases are rare and only of a more or less academic interest. As to the low blood sugar concentration it is well known that there is produced by the lowering of the blood sugar a series of symptoms which may be slight or more severe, culminating in death if the condition is not recognized and promptly treated.

I will make a further remark on hypoglycæmia when speaking of "Insulin." The importance of the estimation of the blood sugar concentration in the diagnosis lies in this, that we depend upon this knowledge for the absolute diagnosis of the disease and it can be stated as a general fact that in the fasting patient a blood sugar content of 0.12% or more indicates a diabetic state and in a patient who has just enjoyed a meal the presence of anything over 0.17% is very suspicious.

It is advisable to have both these readings if possible. When our team is sufficiently strong at the Brisbane Hospital, we follow this plan as it is of considerable importance in the prognosis and treatment of the disease.

I have already said that a blood sugar content of 0.24% is severe and a general statement can be made that the higher the blood sugar, the more severe the disease and the more rapidly fatal it is.

It has been emphasized as to the importance of looking for the disease as a routine and sufficient has been said for the purposes of this evening on the question.

Treatment.

The important question of treatment can now with advantage be discussed and it is assumed that one must have at least a working knowledge of the principles of dietetics. It must be known that a normal blood sugar concentration is about 0.1% and it must be known that the caloric values of carbohydrate, protein and fat are respectively 4, 4 and 9.

There is no necessity for a very extensive knowledge of the caloric values of foods nor is there any need to be a sort of encyclopædia of knowledge as to the various kinds of foods to be used, but it is essential to have a working knowledge of the few foods which are commonly used and on which any ordinary diabetic diet can be founded and built up. One must know, for example, that there are thirty grammes in an ounce approximately or *vice versa* that there are about three ounces in one hundred grammes; that black coffee has no food value and that ordinary beef tea has no food value either, nor has bran, despite popular opinion.

It is also well to remember that the 5% vegetables are very safe articles of diet to prescribe. They can be prescribed with a knowledge that they can do no harm. In this category come lettuce, cucumber, asparagus, silver beet, rhubarb, marrow, celery, mushroom, tomato, cabbage, radish and so on. In the list of 10% vegetables there are beans, beetroot, carrot, oranges, pineapple, turnips and the rest.

Bread and those articles made from flour are the *bêtes noirs* of the diabetic and it is at times a matter of the greatest difficulty to persuade the diabetic to abstain from bread. It is surprising how few diabetics are resigned to be deprived of their bread and I expressly forbid the taking of it unless specifically ordered in the diet of the patient and I am quite convinced that overindulgence in bread is one of the most frequent rocks (literally perhaps) on which many a good diabetic founders. The patient can do without bread quite easily. But it is just as easy to work it in in a properly balanced diet and it can be so adjusted that there is quite a helping of bread as a sort of *délicatesse* at one particular meal.

Diabetics depend very much for their sustenance on fat and fat foods are essential to the well being of the diabetic in their proper proportion. I should have said that sugar in every form is forbidden to the patient and that the value of bread in calories

is carbohydrate 18, protein 3 and fat 0. Saccharine can be substituted as "Saxin" or any efficient preparation. In speaking of fat I am not treating here of high fat diets nor do I intend to and personally I am not a little afraid of the high fat principle, involving as it does the possible precipitation of an acidosis which is the first thing we have to learn to avoid in the prescription of a diet. To the ordinary patient it is a matter of difficulty at all times to keep on a low and less risky fat diet without the superadded danger associated with a high fat one. The fats of which we have particularly to remember the values are butter, bacon and eggs and these contain respectively twenty-five, fifteen and six grammes of fat to the ounce or thirty grammes of food.

Cheese contains over one-third of fat and lean cooked meat about one-sixth. I must, however, refer you to one of the excellent manuals on the subject for further details, Joslin's "Diabetic Manual," Hill and Eckman on the Allen treatment or Huddleson on food for the diabetic, all of which cover the ground more or less fully.

Of the protein containing foods we have meat with eight grammes, chicken with eight grammes, eggs with six grammes, fish with six grammes, cheese with eight grammes to each thirty grammes and so on. It is important to remember the fact that the basis of all treatment is in the diet, no matter how mild or severe the disease and whether "Insulin" is used or not. There seems to be an idea abroad that the use of "Insulin" gives the patient a licence to eat anything according to taste and that in order to counteract excess in diet more "Insulin" can be used. I am certain that this idea is not only erroneous but positively criminal, as it puts the patient in an absolutely false position. It is crude and unscientific treatment and fraught with a very great danger to the patient's life. I have actually seen a patient who as the result of proper treatment became well and was able to return to his alloted task from a state of the most grave *diabetes mellitus*, die miserably in coma from a stupid and senseless orgy of food through the ill advice of well meaning fools. And besides it is a waste of good and expensive material.

In the Allen treatment, that is treatment by undernutrition, there are certain aims to be accomplished and a knowledge of Allen's desiderata is a valuable aid in controlling any case. In the Allen treatment the first step is to starve the patient until he is sugar-free and then by a process of daily increase in diet, to find out the patient's carbohydrate tolerance.

The chief aim of the Allen treatment is to keep the patient well and able to work without depriving him unduly and without subjecting him to undue risks of acidosis and from time to time at intervals of say a week to give the metabolic processes a period of rest by a day of starvation. Since Allen's original work a great deal of investigation has been carried out in the question of metabolism and chief amongst this was the work which emphasized the importance of the carbohydrate in relation to the oxidation of the fat. Indeed it has been said that the fat is burned up in the flame of the carbohydrate, indicating the necessity for a proper balance between the carbohydrate and fat content of the diet in order that the fat in the diet will be completely oxidized and that there will be no ketone bodies in excess.

It is essential to know for the proper balance of a diet the value of the glucose content. This is easily calculated from the total number of grammes in the diet of carbohydrate, protein and fat. Thus in estimating the glucose content it must be remembered that the protein is equal in its metabolism to 58% of its value as glucose and fat to 10% and on the other side it has to be borne in mind that protein yields 46% fatty acid; this has to be allowed for in estimating the production of fatty acid, that is the ketogenic factor.

It is in this connexion that there has been compiled by various workers a series of accurately determined tables and they are within a few calories very much the same for similar individuals. These tables have been constructed to show the proportion of antiketogenic substances to ketogenic substances necessary for health, that is the prevention of acidosis. It requires approximately one part of glucose to 1.66 or two of fatty acid and there are formulæ by which the calculations can be made; these will be dealt with later on.

The first thing that has to be known in the dietetic treatment of diabetes is the basal metabolic requirement of the patient. Without going into extensive details as to the way in which the calculations are arrived at, it is merely necessary to know that the basal metabolic requirement is the total caloric value of the food necessary for a given patient whilst at rest. It follows, of course, that any exertion on the part of the patient must require more calories and has to be allowed for, but *ab initio* it is assumed that the patient is or should be at rest. It requires approximately thirty calories per kilogram of body weight for the average person to keep up his weight and strength, so that a man of my weight, say, fifteen stone or one hundred kilograms, would require three thousand calories of food per day to keep him going.

The basal metabolic requirements are calculated according to the height, weight, age, sex and surface area in square metres. These can be easily obtained by employing Du Bois's chart. The way to use Du Bois's chart is take the weight of the patient in pounds and the height in inches and to find the point where the lines corresponding to these measurements intersect. The area in square metres is indicated at the end of the curve. This gives the area and the basal requirement can be obtained from the table which is associated with the chart. These figures are absolutely essential for the estimation of the correct balance of the diet. Without them it is impossible to compute the correct proportion of carbohydrate, protein and fat necessary to keep the patient well, while a minimum of glucose is used in the process. For this purpose Campbell's formula is used, which is quite simple and easily employed.

In regard to protein it can be said roughly that it requires one gramme of protein per kilogram for the average allowance, often enough much less is allowed, such as 0.6 gramme, quite commonly. It varies very considerably up to 1.5 or more, but for basal reckonings 0.6 gramme is enough. For children, however, two grammes per kilogram is necessary and MacLean allows one as a routine.

The total metabolic requirement is arrived at by multiplying the surface area in metres by the requirement of the given individual according to age and sex. Thus a man of twenty requires 994 calories per square metre. His surface area is, however, 1.72 metres, therefore his total metabolic requirement is 994 multiplied by 1.72, which gives 1,710 calories. Assuming that the patient weighs sixty kilograms and allowing 0.6 gramme of protein per kilogram, the patient is allowed two-thirds of sixty, that is forty. Campbell's formula, the one we use, is as follows:

$$F = \frac{M}{10} - \frac{P}{2} \qquad C = \frac{M - 10P}{30}$$

when F = fat, P = protein, C = carbohydrate and M = basal metabolism. This would give

$$\frac{1,710}{10} - \frac{40}{2} = 171 - 20 = 151 \text{ grammes of fat}$$

and $\frac{1,710 - 400}{30} = \frac{1,310}{30} = 43.6$ grammes of carbohydrate.

Having these data with regard to the required fat and carbohydrate, they can be transcribed into foodstuffs comparatively easily. There are also in use monographic charts and a straight edge which have for their recommendation a great simplicity and a saving in time, in that by applying the straight edge the requirements can be read off at a glance.

It is usual now in the patient with diabetes to depend for treatment on either the Allen treatment, that is undernutrition, or on the system of basal diets. Personally I think they both have a very great value in their respective spheres according to the intelligence of the patient, his circumstances and so on. As a routine at the Brisbane Hospital the basal diet system only is used.

In the case of patients living far away in the country suffering from only a mild type of diabetes, the Allen system is invaluable and the tables used by Allen are easily followed by even the least intelligent of patients, so much so that quite a number of my patients follow the Allen system only and report from time to time as to their well being and the rest of it.

There is a point that I would like to emphasize in the treatment of these patients and that is the necessity for making a daily note of the state of the patient whilst he is under observation, not only of the actual food he is receiving, but its caloric value, the weight of the patient and the content of the urine as to sugar and acetone and diacetic acid, so that it is possible to see at a glance the ratio between the food intake, nutrition of the patient and the possible advent of a state of acidosis.

In the case of the patient treated with "Insulin" it is important to have, at any rate at first, an intelligent nurse who is capable of observing and interpreting the symptoms which herald the hypoglycæmia. I know myself that on more than one occasion I have my attention drawn to the intolerance of the patient to "Insulin" by the nurse in attendance. The procedure we adopt at the Brisbane Hospital is to keep the patient at rest until sugar-free and when the urine has been sugar-free for a few days a gradual increase in the diet is made in easy stages of two hundred calories *per diem* at a time until there has been given a sufficient quantity of food to enable the performance of light work.

It has been found that patients vary very considerably with the effect of a basal diet; some lose weight and some curiously enough gain. Why they should gain is one of the anomalies of this treatment, but there are many things in the antiketogenic-ketogenic factors as yet not known or only imperfectly understood.

Treatment with "Insulin."

Having given in some detail the treatment of *diabetes mellitus* without "Insulin," some reference must be made now to treatment with it. It is necessary as early as possible to determine the effect of the basal diet on the patient, to note whether there is any excretion of sugar on such a diet and to estimate the amount of sugar excreted. The last factor, that is the amount of sugar excreted, is an important one, as sometimes it is used for the estimation of the dose of "Insulin" to be employed. It is not necessarily a very good guide and to me not a very accurate one and I am convinced that the result of experience is of much greater value than a more or less arbitrary amount of "Insulin" prescribed for all patients according to their sugar output.

It is assumed that an intelligent medical attendant will not use "Insulin" except when necessary and this necessity becomes apparent if the patient cannot be placed on a diet sufficient to keep him in good health and doing his daily task; any diet below this will require "Insulin" as an adjuvant to the treatment.

It is, of course, possible to combine the treatment of diabetes on the principle of the Allen undernutrition and "Insulin," but I have not had much experience of the combination and have no information as to the merits or demerits of such a combination.

With regard to the actual administration of "Insulin" let me say a word. All know that it must be given either by the intravenous or the subcutaneous methods and the intravenous method is reserved for those cases in which there is real urgency, coma and so on.

There is no need to inject the "Insulin" deeper than the subcutaneous tissues, deep enough not to affect the skin, but not into the muscles. A peculiar result has followed the administration of "Insulin" in two cases which I have seen, that of a wasting of the subcutaneous fat, so that the limb of the

patient had the appearance of a long standing infantile paralysis. The muscular power, however, was not impaired and apparently only the fat was affected.

On this account and on account of the induration which is apt to follow the repeated administration of "Insulin," there should be a variation of the site of the injection, but as far as my experience goes, there has been, with the exception of the two cases quoted above, no untoward effect in the administration of the substance. Abscesses have been reported, but if ordinary precautions are taken, there is no need whatever to fear any local complications. The effect of giving "Insulin" is very transient. It has been shown that after the administration of "Insulin" there is a reduction in the blood sugar and that this drop takes place shortly after the administration of "Insulin," reaches its height about four hours after the injection; this effect is brought about by the using up of the glucose, whilst the reduction after starvation is supposed to be due to the excretion of the sugar in the urine.

"Insulin" also improves the capacity for storing up glycogen. "Insulin" also affects the oxidation of the fatty acids. The usual reduction of the blood sugar is about 0.08%. Thus three things are accomplished: firstly there is an increased use of glucose, secondly there is the storage of glycogen and thirdly oxidation of fatty acids.

Dosage.

The "Insulin" is administered as stated before by hypodermic injection before meals. The injections are given as a rule one before each meal, that is three times a day, but the administration can be varied to suit the individual. To those patients who are following their employment, it can be given twice a day or once only in certain circumstances.

There is a certain amount of risk in giving the dose of "Insulin" at night on account of the possible development of hypoglycæmia during the night, but it is a very small risk and is unlikely to occur in a properly managed case. However, it may be discreet to give the major doses during the day at the breakfast and luncheon times and to leave the evening dose out altogether or to reduce it.

There are several ways of determining the amount of "Insulin" to be administered, but as I have said before the opinion I hold is that the less used, the better for the patient.

The usual theory as to the effect of the "Insulin" on the function of the pancreas is that the giving of "Insulin" allows the pancreas to have a rest and that thereby the function of the pancreas is restored. A good deal of colour is lent to this theory in practice because it is observed that after the administration of "Insulin" for a time, the need for it becomes less and at times the use of it may be discontinued altogether.

On the other hand I am quite convinced that the administration of "Insulin" can be overdone quite apart from the production of hypoglycæmia, by the possible effect of lessening the output of the gland by the substitution of "Insulin" for the gland hormone, a sort of atrophy from disuse. As to the size of the dose there is a formula often used which is of some value to those not versed in the effects of "Insulin":

$$\frac{\text{Daily excretion of glucose}}{1.5} = \text{Units of "Insulin."}$$

This formula is varied according to the effects of the administration and the dose can be reduced if the urine becomes sugar-free. It is then usual to divide the excretion of sugar in grammes by 2.3. This formula is at best only a comparative guide and is not to be taken as being an infallible ratio.

The only absolute guide is the blood and urine sugar concentration combined with a deal of practical experience and the only way to control the dosage is the close observation of the blood and urine factors and the drawing of proper deductions from them. The tolerance for glucose may undergo quite a remarkable increase. As I have said before, many patients are able after a time to dispense with the use of "Insulin."

"Insulin" should never be administered during fasting and during our early experience when we were more nervous as to its use one or two nasty frights came our way, not because we had any severe cases of hypoglycæmia, but because we happened to have a few more intelligent patients than the average, who knowing the symptoms of hypoglycæmia promptly obliged.

Hypoglycæmia.

Finally, I would like to say a few words as to the immediate harm which may arise from the administration of "Insulin"; this is what is known as hypoglycæmia or "Insulin" shock.

This may be a fatal condition and it behoves every practitioner who is using "Insulin," to bear clearly in mind the train of symptoms which is likely to develope. The condition is usually quite easily recognizable and prompt treatment brings about immediate relief. The symptoms are air hunger, nervousness, pallor, sweating, fainting, delirium and finally coma.

There has been in the patients I have observed a curious mental condition, a sort of disorientation, the patients being quite unaware as to their place in the sun or the bed or even as to their personality. The treatment consists in the prompt administration of carbohydrate in some form, preferably in the form of glucose. For this purpose it is wise to have handy at the outset of the treatment a 10% solution of glucose for administration by the mouth. Failing this cane sugar in any form can be administered either in bulk or in solution, either by the mouth or by the rectum or the glucose can be given intravenously if a rapid effect is required.

The dose of glucose can be as much as a tablespoonful by the mouth and if the patient is not relieved, the dose may be repeated in twenty minutes or so. This is one of the easiest ways of

treating the hypoglycæmia and it is more pleasant and less alarming than the methods detailed above. In the treatment of acidosis and coma it is necessary to give large doses of "Insulin" and to counteract the possible development of hypoglycæmia doses of glucose are administered at the same time.

Reports of Cases.

PRESENCE OF THE LIVER IN THE UMBILICAL CORD OF A NEW-BORN INFANT.

By P. L. Hipsley, M.D., Ch.M. (Sydney)

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Hernia of portions and at times of nearly all the abdominal viscera into the umbilical cord have been recorded, but the following case in my experience is unique.

B.C., a male infant, whose weight at birth was 3.18 kilograms (seven pounds four ounces), was admitted to the Children's Hospital on July 26, 1925, twelve hours after birth.

There was a spherical enlargement of the proximal portion of the umbilical cord, firm in consistency, about 7.5 centimetres (three inches) in diameter at its widest part and 3.1 centimetres (one and a quarter inches) at its junction with the abdominal wall.

In appearance it resembled a large spherical swelling of the cord, none of it being covered by skin.

Under ether an incision was made through the skin at its junction with the sac and on opening the latter the whole liver was found within it and adherent to a considerable portion of it. On separating these adhesions free bleeding was encountered and was arrested by several figure-of-eight catgut sutures. The incision in the abdominal wall was then enlarged and the liver returned within the abdominal cavity, no attempt being made to fix it in position.

The abdominal incision was closed in layers.

The infant made an uninterrupted recovery and three weeks later appeared to be perfectly normal.

An X ray examination, made three weeks after the operation, revealed the shadow of the liver still spherical in shape and situated in the usual position of the right lobe.

Analytical Department.

"MUTHANOL."

"Muthanol" is a bismuth preparation manufactured by G. Fermé of Paris. It is stated to be a hydroxide of bismuth and to contain 0.1 milligramme of mesothorium bromide in each sample. It has been introduced for the treatment of syphilis. The ordinary dose for an adult is two cubic centimetres said to contain thirteen centigrammes of metallic bismuth. The dose for infants is one cubic centimetre. The preparation is put up in glass ampoules. These ampoules have to be shaken until the contents are fully emulsified. The neck of the ampoule is then cut with a file and broken off and the suspension sucked up into a hypodermic syringe.

Chemical Composition.

On analysis undertaken for The Medical Journal of Australia it was found that the contents of each ampoule weighed 2.433 grammes and measured exactly two cubic centimetres. The amount of hydroxide of bismuth was 0.124 gramme which is slightly lower than the reputed amount. Our analyst reports that the bismuth hydroxide is in a colloidal condition with free ions ready to act on injection, that is to say there are no acidic radicals present to hinder true ionic dispersion. He adds that this does not imply that the hydroxide of bismuth would not act as an ordinary electrolyte in an inorganic solution. The presence of a radioactive mesothorium compound was determined.

Clinical Studies.

Various bismuth preparations have been given to patients suffering from syphilis in certain clinics since November, 1922. We have reports of the results obtained from "Muthanol" given to nearly two hundred patients. At one clinic the results appeared to have been as good as those of one other colloidal preparation of bismuth and better than those of four other bismuth preparations. The power of the patient's blood to deflect complement in the Wassermann reaction is rapidly removed under the influence of this preparation even when the patient has not reacted well to mercury or to the arsenobenzol drugs. In congenital syphilis this effect upon the blood serum followed rapidly in twenty-five out of forty patients. Ten patients with early primary lesions who were intolerant to arsenic medication, were treated with "Muthanol" alone. The blood serum of all these patients yielded a reaction to the Wassermann test. The primary sores healed after four to six injections. At this stage no Wassermann reaction was obtained with the blood of eight of the patients. Over a hundred patients with long standing latent syphilis were also subjected to this treatment. Thirty-six patients had had treatment with arsenobenzol drugs and with mercury for periods daily from two to five years. In spite of this treatment the blood serum deflected complement. After one course the serum of twenty patients lost its power to react, while after two courses the serum of three other patients also lost this power. In the remaining thirteen patients no change was effected. Forty-three patients were still under treatment with "914," but the blood serum still reacted to the test. Medication with "Muthanol" alone had the desired effect in sixteen patients and with "Muthanol" and arsenic in a further twelve. Similarly twenty-two out of twenty-eight patients responded to "Muthanol" or "Muthanol" and "606," after "606" alone had proved insufficient.

For syphilis of the central nervous system "Muthanol" has been found to be of great value. The lightning pains of *tabes dorsalis* and the gastric and vesical crises were relieved. The majority of the patients were considerably benefited by the treatment; after four or five injections they gained in weight and in strength. "Muthanol" was also given to elderly subjects with gummatous syphilides. It was held to be unsafe to administer the arsenobenzol drugs to these patients. The lesions healed under "Muthanol," although not at a very rapid rate.

The majority of patients tolerate twelve intramuscular injections given at intervals of one week. A blue line usually appears on the margin of the gums after the tenth to twelfth injection. Many patients have received more frequent injections, but none have manifested any untoward symptoms or sign.

It is the opinion of the clinicians who have reported on the use of "Muthanol" in the treatment of syphilis, that it is a powerful spirochæticide and that it should be used in courses alternating with courses of the arsenobenzol drugs. There is no doubt that efficient bismuth preparations will replace mercury and to some extent arsenobenzol drugs in private practice.

Conclusions.

We have sufficient evidence to enable us to state that "Muthanol" is a reliable preparation of a therapeutically active salt of bismuth in a state of very fine division. It is probably one of the best bismuth preparations available at the present time. It together with one or other of the arsenobenzol drugs should be given in all cases of syphilis.

The distributing agent is Mr. G. F. W. Musson, 88, Hunter Street, Sydney.

The Medical Journal of Australia

SATURDAY, OCTOBER 17, 1925.

Medical Defence.

MEMBERS of the British Medical Association in Australia will read with interest and profit the debate in the Representative Meeting on the proposal that the Council should prepare a draft scheme of individual medical defence and subsequently should ascertain how many members would be prepared to join in its membership. In Great Britain there have been in existence for many years two medical defence societies. It is estimated that the total membership of these two societies is about twenty thousand. This number, however, has to be discounted to some extent because it includes a large number of dentists. Admirable as these two societies are, it appears that a substantial proportion of the medical profession remains unprotected against the dangers arising from an attack on the professional integrity of its members. No matter how well the British Medical Association does its work in regard to collective defence, the upholding of the honour and interests of the medical profession as a whole, the real burden has to be borne by individual medical practitioners. It is usually impossible for a young graduate during the early years of his career to meet the exorbitant costs of a law suit. At times the adequate defence of a professional reputation may be based on the upholding of a principle of far reaching importance. It is therefore not only unwise but even reprehensible for a medical practitioner to fail to protect himself by joining a medical defence society. In Australia we have societies of a similar character. Although they are relatively small undertakings, they have served their purpose well in the past and in the future they will become financially stronger and more powerful.

Dr. Morton Mackenzie gave a full recital of the events during the past half of a century concerning the proposal that the Britsh Medical Association should make provision to offer medical defence to its members. The demand has been insistent from a minority during this long period, but it has not been adopted by a sufficiently large number of members to bring it into the realm of practical politics. The constitution of the Association does not admit of this form of activity. Medical defence stands midway between the legitimate activity of a scientific society incorporated under the *Companies Act* as a company not for profit and the purely commercial activity of an undertaking such as the business of a medical agency. Early in the present century there was a strong movement to alter the constitution of the Association to enable it to carry out many functions that were not enumerated in the objects in the Memorandum of Association. The principal power that was sought, was the power to establish medical benevolent funds. Medical defence was included in the desired new functions of the Association. Both these objectives might have been attained had a charter been secured, although the charter would probably have imposed restrictions on the activities of the Association in other directions. Be this as it may, the application for a charter failed and the Association recast its Memorandum and Articles of Association in the manner best suited to its primary aims and objectives. Had Dr. Morton Mackenzie's motion been carried in the Representative Meeting and had the referendum resulted in a mandate to the Council to proceed with the introduction of the scheme, it would have been necessary for the Association to have instituted a special society or company to conduct the business of medical defence. The majority accepted the amendment from the Cardiff Division and for the present the British Medical Association will not endeavour to organize this undertaking. It will be noted that the Cardiff amendment embraced a proposal to effect a better cooperation between the existing medical defence societies and the British Medical Association.

There is a lesson to be learned from the debate and its result. The British Medical Association was founded for specific purposes and its machinery has been cast along very definite lines. It can undertake many things for the furtherance of medical science and for the maintenance of the honour and

interests of the medical profession. But it has to give a wide berth to all commercial undertakings. The Memorandum of Association contains provision for two undertakings that involve commercial enterprise. Both of these are essential to the objects of the Association. The first is that of printing and publishing medical journals. In the absence of a large endowment a medical journal is compelled to cover a substantial part of the cost of production by the letting of space for advertisements. In addition medical journals, even those that are handsomely endowed, are offered for sale. The commercial aspect of printing and publishing a medical journal is unavoidable and essential. The second undertaking of a commercial nature that a company incorporated as a company not for profit can indulge in, is the holding, selling or leasing of property. Scientific societies have long realized the necessity of owning their own homes. The house of the British Medical Association in the Strand was a very valuable property, but its occupation was rendered feasible only by the expedient of leasing the ground floor to a commercial firm. The Association can let the Great Hall in Tavistock Square for pecuniary gain. These are the only commercial activities permitted. Whether medical defence can be regarded as a commercial activity or not is immaterial. It cannot be undertaken by the British Medical Association. Fortunately other agencies are prepared to carry it out. It is an essential service for the medical profession and every member of the Association in active practice should join the available society.

Current Comment.

GUANIDINE AND HIGH BLOOD PRESSURE.

In November, 1924, we made reference to some work that had been done by Dr. Ralph H. Major in regard to the relationship between arterial hypertension and guanidine. He found that when guanidine was injected into dogs, an increase in blood pressure resulted and persisted for several hours. He then studied the excretion of guanidine bases in the urine of persons suffering from *diabetes mellitus*, chronic nephritis, essential hypertension and in the urine of normal persons. He found that persons with a high blood pressure excreted an amount that was definitely less than that excreted by others. At the same time he found one patient suffering from severe chronic nephritis who gave evidence of considerable protein destruction. This patient manifested a high output of guanidine bases, but had a normal blood pressure.

Dr. Major has published the results of further observations on the same subject.[1] He studied the excretion of guanidine in two patients who suffered from essential hypertension. The patients were treated with digitalis and "Diuretin," the blood pressure fell considerably, urinary secretion was increased and there was an increase in the excretion of guanidine. As these observations suggested that there might be a retention of guanidine during the period of high blood pressure, the blood serum of a large number (not stated) of normal individuals and of patients suffering from arterial hypertension was examined. No increase was found in the guanidine content of the blood of those with high blood pressure. Pursuing these observations further Dr. Major studied the blood guanidine of dogs after the injection of guanidine compounds. He found that while the guanidine content of the blood was increased for two or three minutes after the injection, the excess had entirely disappeared in five minutes, although the blood pressure remained elevated for some hours. It was found in an endeavour to explain these findings that the urine contained no constant increase in guanidine bases and on examination of the various organs that there was no storage of the increase in some tissue. There remained then only two possibilities. Either the guanidine was changed into some other substance which has a prolonged pressor effect, or rapid saturation occurred with destruction of the excess. In regard to the first of these it is pointed out that guanidine is probably transformed either into cyanamide and then into urea or into urea directly; neither of these has any pressor effect. Dr. Major arrives by a process of exclusion at the view that the pressor effect of the guanidine compounds is apparently exerted almost immediately on the neuromuscular apparatus of the smaller blood vessels. He thinks that it is probable that these tissues fix a certain amount of the guanidine and that the excess is very rapidly destroyed.

In considering his results Dr. Major is wisely cautious. He states that his observations suggest that there may be a relationship between guanidine and arterial hypertension. He merely finds that any great excess of guanidine is destroyed. The question is still undecided as to whether high blood pressure is caused by an increased production of guanidine due to an error in metabolism or whether faulty excretion of guanidine by a damaged kidney is at the root of the matter. If Dr. Major's conclusions are correct, it is not unreasonable to postulate the existence in some instances of blood vessels whose neuro-muscular apparatus has been made or is inherently susceptible to guanidine. In any case it is by researches along the lines adopted by Dr. Major that the riddle of arterial hypertension may ultimately be solved.

[1] *The American Journal of the Medical Sciences*, August, 1925.

PRIMARY CARCINOMA OF THE LUNG.

ALTHOUGH secondary malignant growths of the lung are not infrequently seen in clinical practice and the *post mortem* room, it is commonly held that primary carcinoma of these organs is not of common occurrence. Malignant disease may invade the lung from neighbouring structures such as the pleura or those in the mediastinum. Adler in 1911 made an important communication in regard to malignant disease of the lung. He tabulated three hundred and seventy-four cases of carcinoma and ninety of sarcoma. He expressed the opinion that primary cancer arises in the lung substance as distinct from the hilum and held that a malignant growth of the lung is really a bronchial carcinoma.

Ewing has classified pulmonary carcinoma according to their histogenesis into three groups: (i.) Those arising from the bronchial epithelium, (ii.) those arising from the bronchial mucous glands, (iii.) those which take origin from the alveolar epithelium. At the same time he has pointed out that although these tumours can be distinguished by gross anatomical features and by certain clinical characteristics, the specific features belong chiefly to the early stages of the tumours. Distinctive features are lost in advanced tumours, especially those of a more malignant type.

Bland Sutton has pointed out that more attention will be paid to malignant tumours of the lung in view of the attempts that have been made to deal with them surgically. One patient operated on by Lenhartz for a pulmonary tumour survived for eighteen months. Since successful treatment depends as a rule on early diagnosis, any contribution which will help in this regard is of value.

Dr. H. M. Moses has recently reported three cases of primary carcinoma of the lung.(1) In view of the fact that three patients suffering from this condition were admitted to the same hospital within a space of four months, Dr. Moses concludes that the condition is more common than is usually believed. The tumour affecting the first patient was found at *post mortem* examination to be an alveolar epithelioma. Practically the whole of the upper lobe of the left lung was involved. There were no metastases. The tumour affecting the second patient was found to be squamous celled and to have taken its origin from the lining epithelium of a bronchus. Extensive metastases were found in the abdominal organs and other parts of the body. At the *post mortem* examination following the death of the third patient an "abscess" cavity as large as the first was found opening into the right bronchus just below the bifurcation of the trachea. The appearances found on opening this cavity were such that a diagnosis of caseous tuberculosis was suggested. Yellowish nodules resembling areas of caseation were found scattered throughout the remainder of the lung. The neoplasm was composed of squamous epithelium and although the œsophagus was involved to a certain extent, it would appear from the account given that the primary growth occurred in the bronchus. No evidence of tuberculosis could be found. The appearance found is full of interest. Many observers have pointed out that the early manifestations of pulmonary neoplasm may be similar to those of tuberculosis. There is no reason why both conditions could not be present in the one individual, nor is it unreasonable to suppose that a neoplasm might form in the wall of a tuberculous cavity.

In discussing his three cases, Dr. Moses puts up a plea for the use of the bronchoscope in diagnosis. This instrument was used in all three cases and definite and useful information was gained in each instance. A piece of tissue was removed from the wall of the bronchus of the third patient by this means and the epitheliomatous nature of the growths was revealed. He states that X ray examination will not reveal primary growths in the lungs or bronchi in an early enough stage to permit of their removal by radical surgery.

Bronchoscopy may be a means of diagnosis of growths in the larger bronchi, but tumours found in these situations through this agency will most likely be in such a position that radical removal will be impossible. At the same time most clinicians will agree with Dr. Moses that it is necessary to watch closely those who complain of persistent cough without demonstrable cause, those who expectorate blood-stained sputum in which no tubercle bacilli can be found, and those who complain of general weakness and loss of weight and who do not react to the usual methods of treatment.

[1] *The American Journal of the Medical Sciences*, July, 1925.

STANDARDIZATION OF THYREOID PREPARATIONS.

IT is unnecessary to discuss the need for a reliable and simple method of standardizing thyreoid preparations. It is not sufficient to determine the iodine content, for iodides can be added. IN 1909 Reid Hunt suggested the use of aceto-nitrile for the determination of the activity of thyreoid substance. Professor W. Straub undertook at a conference held in Edinburgh in 1923 to investigate the various pharmacological methods of standardization of thyreoid preparations. He now reports that Reid Hunt's suggestions with certain modifications yield reliable results.[1] It appears that 0.9 milligramme of aceto-nitril per gramme body weight is the lethal dose for mice, while 0.675 milligramme does not kill. If carefully dried thyreoid gland substance suspended in saline solution be introduced through a tube into the stomach, recovery follows the intravenous injection of two lethal doses of aceto-nitril. He has found that the optimal effect of the thyreoid substance is obtained by giving 0.2 cubic centimetre of a 5% suspension. The effect is less when either higher or lower concentrations are employed. If mice are given thyreoid gland substance *ad libitum* with their food, the effect is uncertain. Similarly repeated doses should not be used, since the increased resistance to aceto-nitril disappears after four days. Various preparations were tested and those that were found to possess diminished action, exhibited a lessened effect on the body weight and carbon dioxide excretion.

[1] *Deutsche Medizinische Wochenschrift*, January 2, 1925.

Abstracts from Current Medical Literature.

MEDICINE.

Lobar Pneumonia.

GRIEG ANDERSON (*The Lancet*, February 28, 1925) contributes a review of the modern treatment of lobar pneumonia. He emphasizes the danger of carriers of this disease, the Rockefeller Institute workers having shown that virulent pneumococci may be recovered from the air passages of convalescent patients and from attendants. Thus arises the necessity for strict isolation, for the prophylactic swabbing of the throat and so forth and for the adequate disinfection of fomites. The author also emphasizes the necessity for securing sound sleep in the course of the disease. Bromides and other hypnotics are useless for the purpose and reliance must be placed upon hypodermic injections of morphine and atropine. With the exception of digitalis, no drugs are of real value in routine treatment. But digitalis, used early, does seem an aid in warding off failure of the right side of the heart. The writer lays stress on the ominous significance of a falling blood pressure and believes that adrenalin has a definite use when the tension is dropping. The use of alcohol should be restricted to elderly and debilitated patients. Venesection is often advisable at the outset of the disease, particularly in obese patients and signs of commencing failure of the right side of the heart call for the removal of four hundred and fifty to six hundred cubic centimetres of blood. Specific therapy, except against pneumococci belonging to Group I., has not proved beneficial and even here the results are not comparable in efficacy to those obtained by the use, for instance, of antidiphtheritic serum. The patient receiving serum therapy must be sensitized in the ordinary way and the serum must then be used in large doses. One hundred cubic centimetres are injected in the first twenty-four hours and doses of forty to fifty cubic centimetres are given on subsequent days. Vaccines so far have been useless in the treatment of lobar pneumonia.

Diabetic Coma.

NELLIE B. FOSTER (*The Journal of the American Medical Association*, March 7, 1925) discusses the mode of onset, the pathology and the treatment of diabetic coma. It has been stated that three conditions predispose to coma: infections, lapses in diet and failure to use an accustomed amount of "Insulin." Even the minor infections such as coryza, bronchitis and tonsillitis may precipitate coma. It is essential to be on the look out for its onset and to commence prophylaxis on the appearance of the first symptoms. Dehydration is the most important consequence of acid intoxication; it results from the inability of the patient to take fluids either owing to nausea or drowsiness, it results from diuresis due to the high blood sugar content and from loss of water from the lungs due to increased pulmonary ventilation (air hunger). In consequence the tongue becomes dry, the skin loose and the eyes sunken. The necessary measures to combat this state are to provide fluid in the shape of normal salt solution. This is best given subcutaneously, since the intravenous method might overload the heart and rectal administration is too slow. The intraperitoneal route can also be employed satisfactorily. In order to burn up the fats glucose must be administered intravenously; as much as 20 grammes of glucose in the form of a 50% solution can be injected every two hours till the patient can swallow orange juice. Forty to one hundred and fifty units of "Insulin" should be injected as a first dose, the patient's bladder should be catheterized every two hours and if sugar is found in the urine more "Insulin" should be given. This procedure must be continued until the urinary sugar diminishes. Care must be taken at this stage not to produce hypoglycæmia; the best method is to use abundant "Insulin" and sufficient glucose intravenously. Part of the first dose of "Insulin" should be given intravenously. It is noted that myocarditis is evident in all patients who die in diabetic coma; therefore caffeine should be used or "Oriabain." If there is no improvement in the patient's condition in two hours a second dose of "Insulin" as large as the first dose should be given and then twenty to twenty-five units every two hours till the sugar in the urine diminishes. As soon as the patient is conscious, hot coffee or hot broth in quantities of sixty to ninety cubic centimetres (two to three ounces) every fifteen minutes should be given by mouth. After two hours lemonade sweetened with glycerine and as much orange juice as the patient craves should be given. During the first twenty-four hours milk and orange juice only should be given, one litre of milk with the juice of six to ten oranges. The ketonuria may disappear in one or several days. When clinical acidosis is no longer evident, treatment is carried on as in an ordinary diabetic case.

Oxygen Therapy in Pneumonia.

A. E. GUEDEL (*The Journal of the American Medical Association*, May 16, 1925) describes a method of oxygen administration in use in the hospitals of Indianapolis for patients with pneumonia. A commercial oxygen cylinder of 3,113 or 6,226 litres (one hundred and ten or two hundred and twenty cubic feet) capacity is used; to the cylinder is connected a pressure reducing gauge graduated so as to indicate a flow of one to twelve litres per minute. From this gauge the oxygen is carried by a 0.6 or 0.9 centimetre (quarter or three-eighths inch) rubber tube 1.5 or 2 metres (five to ten feet) long into a tent placed over the patient's head. The tent is made by cutting in half a sixty or seventy-five centimetre (twenty-four or thirty inch) wooden barrel hoop, the two halves are crossed and tied together to make the tent frame, roughly hemispherical, this frame is set over the patient's head and covered with one thickness of an ordinary muslin sheet, the excess sheet being tucked in about the bottom of the frame to prevent gross leaks. Sometimes a ventilation aperture about ten centimetres in diameter is left at the most dependent part of the tent. The tube is inserted at the top or side of the tent so as to deliver the oxygen near the patient's face. Analysis of the gases within the tent showed an average of 32% of oxygen and 4% carbon dioxide. With one thickness of muslin there is no excessive warmth and no sense of suffocation as a rule. Oxygen is administered as soon as there is any cyanosis of the finger nails and is kept up continuously for one day up to two weeks. The rate of flow is the slowest rate at which the finger nails can be kept pink, this being a simple way for the nurse to estimate the extent of cyanosis. In most cases three to four litres per minute are sufficient. During necessary interruptions the finger nails are watched for cyanosis. If they remain pink when the oxygen is discontinued it can be left off till they again become cyanosed. Relief from dyspnœa and cyanosis is obtained by this method. For children the tent is larger so as to envelop the whole body and is draped over the sides of the cot, a larger flow of oxygen then being necessary. Commercial oxygen is cheaper than medical oxygen and is equally efficacious. The author considers the method has been satisfactory and recommends its general adoption on account of its simplicity and its great advantages over the open method of oxygen administration.

Amœbic Bronchitis and Asthma.

A. PANAYOTATON (*Wiener Medizinische Wochenschrift*, April 11, 1925) describes two cases of chronic bronchitis and asthma due to the *Amœba histolytica*. In both patients the bronchitic symptoms were greatly accentuated, especially as regards temperature and hæmoptosis. Following on the discovery of the amœba in the sputum energetic emetin treatment caused a rapid disappearance of all symptoms. Adrenalin was added to combat the asthmatic tendency.

Incidence of Paralysis and Tabes Following Syphilis.

K. WILMANNS (*Klinische Wochenschrift*, June 11, 1925) after examining the statistics from numerous countries comes to the following conclusions regarding the incidence of paralysis and *tabes dorsalis* following syphilitic in-

fection. In countries where the vast majority of the inhabitants are infected and where little treatment is carried out severe cutaneous and bone lesions are noted. Metasyphilitic lesions are very rare indeed. In civilized countries where treatment is much more thorough, extensive infections of the skin and mucous membranes as well as tertiary lesions are not common. *Tabes dorsalis* and paralysis on the contrary have been noted to be increasing out of all proportion. They usually occur in patients who have had few early symptoms. It is doubtful whether energetic antisyphilitic treatment lessens the incidence of these metasyphilitic infections.

Scarlet Fever.

G. F. DICK and G. H. DICK (*The Journal of the American Medical Association*, May 16, 1925) have reported further experiences with the skin test for susceptibility to scarlet fever and with the preventive immunization with scarlet fever toxin. The toxin was obtained from filtrates of cultures of the hæmolytic streptococci that had produced experimental scarlet fever in human beings. The sterile toxin injected into susceptible persons produced malaise, vomiting, fever and the rash of scarlet fever, preceded by an incubation period shorter than that of scarlet fever. The toxin is obtained by inoculating plain broth with pure cultures of scarlet fever streptococci, incubating for four to six days and filtering; the filtrate must be sterile. One cubic centimetre of toxin is diluted with normal salt solution to one or two litres and skin tests are made with 0.1 cubic centimetre of various dilutions on the arms of susceptible persons. When a dilution has been obtained which gives reaction corresponding to the standard solution previously prepared, this dilution is tested on twenty susceptible and ten immune persons. Pseudo-reactions occur frequently if much foreign protein is present in the toxin, especially if the medium used has contained horse blood. Skin reactions are mild in susceptible persons. They are still evident after twenty-four hours. If the eruption has entirely faded before that time, it is held that no reaction has taken place. An area of reddening more than one centimetre in diameter is regarded as a positive response. Further observations that absence of reaction indicates immunity and that a positive response indicates susceptibility were made. Immunization was carried out by giving as total dosage from one hundred to twelve thousand five hundred skin test doses to susceptible persons in graduated doses at intervals of five to seven days. A severe reaction should not be produced. Sufficient dosage was indicated by no reaction. The larger doses gave much better immunity than small doses of one hundred to one thousand skin test doses. A first dose of five hundred, and a second of one thousand five hundred and a third considerably larger dose was found to produce no undesirable reactions. There was always a local swelling and reddening lasting one to two days. General reactions were rare and mild. Malaise, nausea and erythema occurred at times after the first dose only. The reactions were milder than those occurring after immunization to enteric fever or diphtheria. Active immunity occurred within two weeks and lasted at least one and a half years. Two hundred and six susceptible nurses were immunized as above before undertaking the care of scarlet fever patients; none contracted scarlet fever. Four hundred and five susceptible persons who were temporarily exposed to scarlet fever, were similarly inoculated and none contracted the disease.

Hypertension and Nephritis.

F. M. ALLEN (*New York State Journal of Medicine*, May, 1925) discussed hypertension and the treatment of nephritis. He points out that cardio-renal-vascular disease is the first among the causes of death in adults. Infection (any acute or chronic disease in which bacteria or their toxins enter the blood) is known to be a cause of heart disease. Scarlet fever, tonsillitis and other acute fevers sometimes give rise to acute nephritis which may pass on to chronic nephritis. Focal infections in the teeth, sinuses and so forth can apparently cause kidney disease. Hypertension is sometimes due to focal infection and syphilis can cause arteriosclerosis and hypertension. Disorders of the heart, kidneys and blood vessels are so closely associated that a common ætiology is easily assumed and it is now generally accepted that these disorders are due to different infections or intoxications. Other poisons such as tobacco, lead, mercury and alcohol and exposure to cold are debatable causes. Heredity is a predisposing cause of hypertension and apoplexy, but heredity is not the cause in the great majority of such conditions. Modern civilization with its stress and strain has not been proved to be a potent cause of arterio-renal disease. These diseases seem more prevalent because diagnosis has improved. Statistics are better kept and people live to middle and old age more often. Endocrine disorders have not been definitely shown to cause arterio-renal disease, though hyperthyreoidism and diabetes are often associated with hypertension. Prophylaxis should consist in avoiding and treating infection whenever possible and in giving a low protein and salt content in the diet to all patients with nephritis until it is shown that these food factors are no longer aggravating the renal disorder. Alcohol and tobacco excess should be avoided though these poisons are not proven to be directly connected with arterio-renal diseases. These diseases were classified recently by Volhard as follows: Renal disease with nitrogen retention tending to end in true uræmia; renal disease with œdema albuminuria and anæmia, but without hypertension or nitrogen retention; high blood pressure tending toward death by apoplexy, heart failure or pseudo-uræmia. All combinations may occur between these three forms of disease. Renal function tests are not of much value to the general practitioner and there are generally other reliable methods by which he can arrive at the diagnosis and prognosis. As regards diet tests the best test is to note the effect of high protein diet on the blood nitrogen concentration and reduce the protein so as to keep the blood nitrogen low. If low protein diet does not keep the blood nitrogen down, the prognosis is bad. Similarly if there are œdema and hypertension little salt should be given. Alkaline injections to relieve supposed acidosis of uræmia has proved valueless; it is more useful to endeavour to keep the urine nearly neutral. High protein diets, calcium chloride and "Novasurol" (a mercurial drug) has not been of much use in removing œdema when real salt restriction has failed. The results of treatment by protein and salt restriction in cardio-renal disease have been very satisfactory in reducing blood pressure and preventing the onset and progress of complications such as retinitis, renal asthma, apoplexy, cardiac failure; but if the blood pressure is not reduced, the complications cannot be prevented. Salt free diet is useful in heart failure, *diabetes insipidus* and nocturnal enemesis of children.

Scarlatinal Antitoxin.

C. L. THENEBE (*Boston Medical and Surgical Journal*, May 14, 1925) records the results of treatment of twenty-two patients suffering from scarlet fever with Dochez's anti-scarlatinal serum. The serum was administered intravenously in doses of ten to one hundred and fifty cubic centimetres. There were no unpleasant reactions and no rise of temperature occurred after the injection. For control purposes eighteen patients were treated at the same time without serum. In general it appeared that the temperature fell to normal and the rash faded much earlier when serum was given. Death occurred in three cases in which the toxæmia was great; serum had been administered to the three patients. Complications occurred, but seemed less frequent after serum administration, but the giving of serum did not affect the complications once they were in evidence. The author considers it logical not to expect the serum to have any good effect in treatment of local infections such as arthritis, adenitis, conjunctivitis *et cetera*, but he claims that its main effect is seen during the stage of toxæmia. He recommends a further trial of the intravenous route instead of the intramuscular route in giving the serum on account of the smaller dose necessary, the quicker action and the lack of untoward effects.

British Medical Association News.

SCIENTIFIC.

A MEETING OF THE VICTORIAN BRANCH OF THE BRITISH MEDICAL ASSOCIATION was held at the B.M.A. Building, East Melbourne, on August 5, 1925, DR. R. J. BULL the Vice-President, in the chair.

Cancer Research.

DR. A. H. THWAITES read a paper dealing with "Recent Advances in Cancer Research" (see page 471).

PROFESSOR P. MACCALLUM in opening the discussion said that the Branch was greatly indebted to Dr. Thwaites for his able and comprehensive review of an exceedingly difficult subject.

The earlier part of the paper emphasized more than anything else perhaps the importance of the immunological aspect of cancer research. There were many points of similarity between bacterial infection and tumour growth, the essential difference being that the unit in one case was the bacterium, in the other the autonomous cell. The "tumour" in the case of bacterial infection was a reaction phenomenon on the part of the body cells; in the case of invasion by the autonomous cell the tumour consisted mainly of the results of that cell's multiplication. The reaction against bacteria was one against exogenous invasion, that against a neoplasm against endogenous invasion. The bacterium was an individual, the cell a unit in a community of cells which had taken on itself to behave as an outsider in that community, to behave in fact more like a bacterium. Cells were inherited; bacteria were not. They were presented to infants gratuitiously.

Just as certain powers of resistance against bacteria were inherited, so also, as had been shown experimentally, varying powers of resistance to tumour growth might be inherited and transmitted according to Mendelian laws. It had further been shown by the experimental transmission of tumours by transplantation that successful growth at one site might increase the resistance of the subject to implantation in another site of the same tumour. The enhanced resistance was also manifested in less degree to other tumours. The increased powers of resistance were dependent on the presence of the tumour and were not lasting since soon after removal of the growth resistance returned to its former level. These observations possibly furnished a measure of explanation of the relative rarity of multiple tumours.

Parallel facts might be cited from bacteriology. The parallel might be extended to the invasive power and special proclivity to cell division and the pathogenicity and virulence of microorganisms, to the limitation of growth in both cases by the products of active growth, to the variations in resistance to destructive agents in accordance with the age of the cells, to the toxic effects of death of bacteria and of tumour cells and to the effects of dosage in the immunity produced by such disintegration.

He did not wish this parallelism to be understood as in any way supporting the idea of a microorganism as the causal agent in cancer; it emphasized rather the autonomy of the cancer cell.

Knowledge was lacking as to why the autonomous cell assumed autonomy. That microorganisms as chronic irritants or as persistent destroyers of tissue and stimulators of reaction might act in an accessory capacity was admitted. Growth activators and specific factors dependent on the cell had to be called in to aid in framing an explanation of the neoplastic process. It was anticipated that the recently announced work of Gye and Barnard would throw light on these factors and the relationship to accessory factors.

Dr. Thwaites had paid a tribute to the work of the physicists in analysing the components of the radiations used therapeutically against cancer. They wanted a complete range of wave lengths and a knowledge of their effects on different tissues. It was now possible to control wave length, intensity and time and use available instruments with a precision the lack of which hitherto had been responsible in a large manner for the disappointments many had felt from the dashing of their too high hopes.

Dr. Thwaites had put before them in a concise manner the degrees of effect which might be produced by graded dosage, nor had he glazed over the limitations of radiological technique which worked in a fine margin of difference in susceptibility between normal and tumour cells and which was specially prone to affect lymphoid and blood forming tissue and special glands.

Professor MacCallum said that he wished to emphasize one point to which Dr. Thwaites had made reference, namely, the question of diagnosis in relation to the method of election for treatment. It spoke volumes for the radiologist that with the handicaps of early limited knowledge of the physics of the agent he was using and of the confinement of his activities to patients beyond the help of the surgeon so large a tumour field should now be recognized as rather peculiarly his.

Early diagnosis was a subject of clinical research of which all recognized the importance, but it seemed to him that too little was attached to the potentialities of differentiating types of tumour growth. Histology both during life and *post mortem* could give valuable assistance in this regard. Too often the point of view was: "Is the tumour innocent or malignant?" when the question should certainly have been: "What is the biological history of this form of tumour?" Many tumours certainly malignant remained localized, others metastasized readily. Knowledge of such peculiarities was of prime importance to the surgeon and in his opinion every surgeon should be a competent histologist or in close contact with one.

To the radiologist who desired to know the effect of his treatment on various forms of tumour, this question was no less important. It governed his method and determined his field of usefulness. Information gained by the histologist regarding the effects to be anticipated from irradiation of different forms of tumour growth, their state of activity and so forth might modify the importance he would attach to the details of the histological picture.

In conclusion Professor MacCallum said that an increase in the frequency of combined efforts on the part of surgeon and radiologist would probably lead to more satisfactory results than each keeping to his own department. He would enter a plea for cooperation in clinical therapeutic research between surgeon, radiologist and histologist; the activities of such teams should further knowledge and increase the number of happy results, while waiting for and contributing to the results of immunological and other research.

DR. H. FLECKER said that he wished to congratulate Dr. Thwaites upon his comprehensive survey of a very large subject.

The effect of irradiation in inducing the resolution of neoplasms might be stated roughly as one of three processes: (i.) autolysis and absorption by leucocytes such as was seen in the treatment of lymphosarcoma; (ii.) proliferation of fibroblasts with resulting incarceration and perhaps ultimate degeneration of the tumour cells; (iii.) direct lethal or necrotic action upon the tumour cells themselves. Of late much less importance had been attached to the last mentioned mode of action and as Dr. Thwaites had emphasized, the trend of recent opinion was that the reaction of the tissues themselves played a most important part in the production of immunity. It must be understood, however, that in treatment by irradiation, even when the attack on a local primary growth might be particularly successful, it was very rare for any distant metastatic focus to be favourably affected unless it also had been irradiated.

If Dr. Thwaites's paper did no more than stimulate the interest of the medical profession in Melbourne and particularly the teaching bodies in non-surgical methods of treating malignant disease, it would be very valuable Until three years previously it had been the custom to discharge surgically abandoned victims of cancer from the general hospitals and arrange for their admission to the Austin Hospital, a process which at the best took several weeks and often many months. Those who survived

this period, were received into a hospital containing three hundred patients all of whom were under the care of a single resident medical officer, there being no honorary visiting staff. Those conditions had since been very much improved, but there was room for further advance. What success had been attained by improved methods of treatment had been demonstrated at the clinical meeting of the Branch at the Austin Hospital in March, 1925.

Dr. C. H. Kellaway said that he had listened with particular interest to Dr. Thwaites's able summary of the biological aspects of cancer research.

It would be a long time before the problem of the inheritance of cancer in man would be elucidated in a degree approaching that achieved by Miss Slye in her work upon the hereditary transmission of malignant disease in animals. It was to be remembered that Miss Slye in her experimental work had by inbreeding of the animals developed a highly cancerous stock. Obviously parallel conditions could not exist in the human subject and here was another instance for the exercise of that caution urged by Dr. Thwaites in applying conclusions drawn from animal experiments to human beings.

Dr. Colin MacDonald said that he would like to ask pathologists present what were the accepted modern views on the metastasis of carcinoma in bone as he thought this subject was of interest from the points of view of radiographic interpretation and radiotherapy.

The value of Sampson Handley's brilliant work on the local spread of cancer of the breast by lymph channel permeation was universally recognized, but some of his disciples amongst the British teachers appeared to hold the view that bone metastases also were almost invariably due to lymphatic permeation. There appeared, however, to be a considerable amount of evidence that embolic dissemination by the arterial and capillary circulation was a frequent cause of bone carcinosis.

Active amongst the British advocates of the frequency of dissemination by the blood were Piney, Director of Pathology at Saint Mary's Hospital, and Sir George Beatson, of the Glasgow Cancer Hospital. Piney believed that bone metastases always occurred first in the bone marrow and no observer had yet been able to demonstrate the presence of lymph vessels in this structure. He explained that emboli lodged in the bone marrow by reason of the widening of the bed of the blood stream; the rate of flow was thereby decreased and the deposit of emboli rendered easy. Embolic settlement in the bone marrow also accounted for the distribution of secondary growths. They rarely occurred in the distal bones of the limbs because here there was usually no red bone marrow. They occurred regularly in the pelvis, spine and ribs where most of the red bone marrow of the adult was to found.

Piney contended that the pseudopernicious blood picture often found in bone carcinosis could only be explained on the ground of intravascular trauma by emboli. He pointed out that such pseudopernicious picture was found not only in the classical instance of carcinoma of the stomach, but occurred irrespective of the site of the primary growth provided that bone metastases had developed.

Dr. MacDonald said that his experience of radiotherapy in the palliation of cancer, gained while working as assistant to Robert Knox and Hector Colwell at King's College Hospital, might be thus summarized. With deep therapy alone the results were so inconsistent that surgeons could hardly be expected to place much reliance upon it; with radium the results were good, but much the best results were obtained by the combination of radium and X ray therapy. The earlier hopes that X radiation would accomplish all that radium could do did not appear to have been realized.

Both English and Continental workers seemed agreed on the value of postoperative prophylactic radiation in mammary cancer. It had been shown, however, that the best results were obtained not with deep therapy, but with medium voltages represented by 130,000 to 150,000. The Erlangen technique and the lethal dose were being discredited on all sides.

Knox attached great importance to repeated examinations of the blood as a guide to treatment. Believing that blood dissemination was a frequent and early complication he always asked for a radiogram of the chest and frequently of the pelvis and spine before commencing radiation. He had demonstrated that a tumour might acquire a reduced sensitivity to a certain wave length if it be continued for long and that the response improved with a change in the wave length.

Ultraviolet light appeared to be a useful adjunct in the treatment of carcinoma, for the clearing of local sepsis in the case of fungating growths and for stimulating the immunity reaction to which Dr. Thwaites had referred.

Dr. Thwaites had appealed for a more exact analysis in radium technique; on the same lines Professor Sydney Russ had strongly opposed the term "milligramme-hours." He had shown that though the product of different intensities acting for different times might be numerically equal, their biological actions might be greatly at variance.

Dr. R. J. Bull said that as it was not the practice of the Branch to record formal votes of thanks he wished from the chair to express sincere appreciation of Dr. Thwaites's admirable paper.

Dr. Thwaites had been the first to hold the cancer research scholarship endowed by Sir John Grice and supplemented by the Victorian State Government and it was apparent that he had maintained a live interest in the subject of malignant disease.

Dr. Bull said that as the hour was late he would not prolong the discussion further than to remark that for many years he had wondered if efficient curative treatment of cancer might not be perfected before the obscure problem of its ætiology had been solved.

Dr. Thwaites had pointed out that there were many points of analogy between benign and malignant growths and he was reminded of a remarkable tumour which came under his observation in conjunction with Sir Harry Allen some years previously. It had occurred in a female patient, the primary growth being located in the pelvis. Metastatic deposits occurred in the form of numerous subcutaneous nodules and dissemination had been found in the liver and other viscera. The histological sections had not in the least resembled those of a malignant neoplasm, but in the absence of the *post mortem* information would have been interpreted as those of an acellular encapsulated myxofibroma.

He had been very interested in the arguments advanced by Dr. Thwaites relative to the hereditary transmission of cancer.

Dr. Thwaites in reply expressed his thanks for the kind reception accorded his paper. He felt that he should offer an apology for the time he had occupied, but the subject was not one that could be dealt with briefly.

Although his remarks on the subject of the treatment of cancer had been largely confined to radiotherapy, he wished to remind them that at the outset of the section of his paper dealing with treatment he had said that operative measures still provided means of the first importance in attacking the majority of malignant growths in their early stages. He did not wish his detailed discussion of radiotherapy to convey the impression that he considered that there was no scope for surgery in the future treatment of malignant growths, but he did consider that there was little if any prospect of further improvement in operative methods used alone.

The ideal was organized team work, by means of which all the prospects might be weighed before decision was made regarding the particular line of treatment to be adopted in each individual instance.

He recognized that in trespassing in the field of immunity he was treading on dangerous ground, but Professor MacCallum had commented very sympathetically. He had been much interested by the parallelism and points of contrast drawn by Professor MacCallum between bacterial invasion and the invasion of malignant growth. He had contrasted the exogenous bacterium with the endogenous autonomous cell.

The observations of Fischer, of Copenhagen, on autonomy of cells were very interesting. This worker had demonstrated in tissue cultures *in vitro* that isolated normal cells did not divide. It appeared that the normal cell could undergo division only when in contact with a group of

its kind and then division occurred in groups and at regular intervals. Isolated malignant cells on the other hand were capable of division which proceeded at a rate determined by the suitability of the conditions in which they were placed.

He wished to urge very strongly the necessity for fuller cooperation between surgeon, radiologist and pathologist. He was greatly impressed by the efficient team work in operation at the Middlesex Cancer Hospital where regular conferences were arranged between all members of the staff. At the Memorial Hospital in New York team work was still further advanced.

He was of opinion that it was only in special cancer institutions that patients benefited to the maximum from present day methods of diagnosis and therapeutic technique. His own observations in London, Paris and New York had given him the impression that the standard of results in the treatment of cancer reached in the general hospitals was not as high as that obtaining in special institutions.

He appreciated the kind remarks of his friend Dr. Kellaway and was very glad to have the general endorsement of so keen and able a critic as the Director of the Walter and Eliza Hall Institute.

Dr. Flecker had stated that the immunity reaction in the tissues which was considered to result from irradiation, was local only and that it was very rare for a metastatic growth to undergo recession even after particularly successful irradiation of the primary growth. In this connexion he would point out that Knox as long ago as 1915 had noted that often a secondary growth retrogressed step for step with the primary which alone was irradiated directly. Other evidence also existed that the immunity reaction stimulated by irradiation was general as well as local.

The three modes of action of irradiation in inducing the resolution of neoplasms mentioned by Dr. Flecker represented the views which until recently were adhered to by the workers at the London Radium Institute. This Institute had been slow to appreciate the advance represented by the work of Regaud, but he had noted in the last report that the London Radium Institute was adopting Regaud's methods and standards and seemed to have accepted the conception of specific immunity reactions as against the merely necrotic effect of irradiation.

The advantages to be gained from an institute of radiotherapy in Melbourne had been emphasized from time to time, but why limit its scope to radiotherapy? Would it not be better to strive for an institute equipped with all the means of diagnosis and treatment of cancer?

With reference to Dr. MacDonald's remarks on the dissemination of carcinoma by lymph channels, Dr. Thwaites said that any exaggeration of the importance of this mode of spread was to be attributed not to Sampson Handley but to some of his supporters. He had observed great benefit in several cases from the addition of ultraviolet irradiation to X or γ irradiation.

In conclusion Dr. Thwaites said that he considered that the best apparent hope for the future lay in the improvement of radiological technique. At present the methods and standards of Regaud were far the best.

A MEETING OF THE VICTORIAN BRANCH OF THE BRITISH MEDICAL ASSOCIATION was held in the Medical Society Hall, Albert Street, East Melbourne, on September 16, 1925, DR. H. DOUGLAS STEPHENS, the Vice-President, in the chair.

The Treatment of Gonorrhœa.

SIR JAMES BARRETT exhibited a motion picture film entitled "The Treatment of Gonorrhœa in the Male."

He intimated that the original film had been prepared for the British Medical Association in London and that the copy he was about to show had been purchased jointly by the University of Melbourne and the Australian Society for Fighting Venereal Disease. The film would be under the control of the University. Hitherto the Society for Fighting Venereal Disease had restricted its propaganda to those efforts that would carry a strong popular appeal, but the present film was technical in character and should be of instructive value to students and practitioners. He anticipated that all would agree with him that thoroughness was the essence of the measures detailed in the film. The present occasion was the first release of the film in Australia.

The film, which occupied about an hour and a half in showing, provided an excellent demonstration of approved and up-to-date measures in the treatment of gonorrhœa and its complications in the male subject.

DR. H. DOUGLAS STEPHENS expressed the appreciation of the Branch of the opportunity afforded by Sir James Barrett for medical practitioners to view the film. It could not fail to prove of great value for teaching purposes.

NOMINATIONS AND ELECTIONS.

THE undermentioned have been nominated for election as members of the New South Wales Branch of the British Medical Association:

Clough, George Miller, M.B., Ch.M., 1924 (Univ. Sydney), Springwood.
Graham, Alexander William, M.B., Ch.M., 1924 (Univ. Sydney), Merriwa.

Medical Societies.

ALFRED HOSPITAL CLINICAL SOCIETY.

A MEETING OF THE ALFRED HOSPITAL CLINICAL SOCIETY was held on June 30, 1925, at the Alfred Hospital, Prahran, MR. FAY MACLURE, the President, in the chair.

Bulbar Paralysis.

DR. J. R. BELL presented a female patient, aged sixty-two years, with weakness of the muscles of the right side of the face, wasting of the right trapezius, right-sided hemiatrophy of the tongue and right-sided palatal paresis. Eighteen months previously she had noticed anæsthesia and difficulty in swallowing and there had been regurgitation of fluids through the nose. These symptoms had gradually lessened in severity. In the ensuing year she had lost twelve and a half kilograms in weight. On examination no abnormal neurological signs had been discovered other than general hyperactivity of the tendon reflexes. The systolic blood pressure had been 160 millimetres. No reaction had been obtained with the blood serum to the Wassermann test. The *fundus oculi* had proved to be normal. The physical signs had become definitely less severe than when the patient had first come under observation three months before. The only therapeutic remedy that had been used, was iodide of potash. The diagnosis was bulbar paralysis.

Paget's Disease.

DR. P. M. REID showed a male patient, aged fifty-eight years, who had come to the Out-Patients' Department, complaining of pain, swelling and heat in the right leg from the knee to the ankle. He had stated that for two years he had suffered from a sensation of weight in the limb and from pain when he used it. He had also noticed that the right shin bone was becoming bowed. His general health had been satisfactory. On examination a cellulitis of the soft tissues was found together with considerable curving of the tibia. The inflammatory condition subsided after the application of hot, moist dressings. After the swelling had disappeared, the great thickening of the tibia and its bowing could be determined. No change had been noted in any other bone; the skull had not increased in size. X ray examination revealed great thickening of the compact bony tissue and a widening of the medullary canal of the tibia. The cancellous bone of the head of the tibia had become disorganized; this had given rise to a smoky, fluffy appearance to the shadow of the bone, which extended to the narrow canal. A skiagram of the skull had been taken. In it some thickening of the diploe was seen in the occipital region. From the radiographic evi-

dence the diagnosis of Paget's disease had been made. Dr. Reid said that in Paget's disease the thickening of the compact bone was due to a replacement of the true bony structure by a fibro-calcareous tissue. The smoky appearance in the marrow space was due to a true fibrosis of the marrow. In regard to the ætiology of the condition, nothing definite was known. Struthers and Dawson, of Edinburgh, had suggested in a recent communication on the subject that it was of endocrine origin. They had found an adenoma of the parathyreoid gland after death in a subject who had suffered from *osteitis fibrosa cystica*.

Mr. A. J. Trinca exhibited a specimen of *osteitis deformans* from the hospital museum.

Dr. G. E. Foreman remarked that the patient had a slight bowing of the shoulders. This was a symptom which seemed to him to add strength to the diagnosis.

Diathermy.

Mr. Balcombe Quick showed a female patient, aged sixty years, on whom he had operated for carcinoma of the tongue nine months previously. About half of the tongue had been removed by diathermy. The cervical glands on both sides had been removed; the dissection had been carried out by means of the diathermy knife. Healing had been rapid and up to the time of the meeting there had been no sign of recurrence. Mr. Quick said that the knife was most effective when the dissection was carried out along the connective tissue planes; the muscles were cut across the long direction of their fibres while they were under slightly increased tension.

Mr. A. J. Trinca called attention to a man, aged fifty-three years, who had had chronic ulceration of his lower lip for many years. Under the tender care of a charlatan the ulcer had begun to progress rapidly and to fungate. A clinically typical epithelioma involving about three-quarters of the lower lip had been present. The removal of this growth in the ordinary way would have necessitated an extensive operation. On June 11, 1925, Mr. Trinca had removed the growth with the diathermy knife. Healing had been so rapid that on June 25, 1925, he had been able to bring together the edges and to suture them. Primary union had followed, as was seen at the meeting five days after the plastic operation.

Mr. Trinca's second patient was a woman, aged fifty-four years. She had had a small epithelioma of the lower lip for six months. This had been treated by diathermy. Within a month it had been almost impossible to detect any sign of the previous trouble. Mr. Trinca said that he did not consider that removal of glands was a scientific procedure. If the glands were involved, surgical interference was hopeless. If they were not involved, surgical removal was unnecessary.

Dr. J. R. Love showed two patients. The first was a man, aged sixty years, who had come to the Out-Patient Department in April, 1924, with a warty growth in the floor of the mouth near the frenum. This had been excised and the base had been deeply burned by diathermy. The pathologist had reported that the growth was a malignant papilloma. In February, 1925, the man had returned with a small ulcer on the right margin of the tongue. This had been treated in the same way as the first lesion. The pathologist had reported that the ulcer was a squamous celled carcinoma. It was noted that there was no evidence of any local disease at the time of the meeting. The scar was very slight. The cervical lymphatic glands appeared to be normal. Dr. Love remarked on the rarity of the occurrence of two distinct types of carcinoma in the mouth. The result up to the time of the meeting was excellent.

Dr. Love's second patient was a male, aged fifty-eight years, who had come to the hospital complaining of a chronic ulcer of the face situated just to the left of the nose. He had recognized it as a rodent ulcer. Its diameter had been about twelve and a half millimetres. Dr. Love had treated the ulcer with diathermy about a year previously. After some months the man had returned and it had been seen that the ulcer had recurred. The new lesion had been small. It had again been treated with diathermy. No signs of recurrence had appeared since that date. Dr. Love stated that he felt sure that more radical measures in the first instance should have prevented the possibility of recurrence.

Dr. F. K. Norris gave details of a case of unresolved pneumonia in a child, which he had treated with diathermy. The child had come to the hospital in January, 1925, suffering from pneumonia affecting the right lung. Skiagrams taken five, seven and eight weeks after the onset of the illness were shown. It was seen that one lung was abnormally opaque to X rays. Daily treatment with diathermy had then been instituted and immediate improvement had followed. Skiagrams had been taken one week after the institution of treatment by diathermy. From them it was seen that a considerable diminution of the shadow cast by the right lung had taken place. The child had left the hospital after a time, apparently cured.

Mr. H. C. Trumble presented two patients. The first was a man, aged fifty-nine years, with an extensive carcinoma involving the greater part of the lower lip and spreading on to the right cheek. A lantern slide was projected on the screen depicting the condition one month prior to operation. The lesion had been a foul, fungating ulcer. It had caused the man much discomfort and had been extremely painful. The whole of the involved area had been removed by means of the diathermy knife. After the operation there had been no pain. Healing had been extremely rapid. One month later there had been no sign of a carcinomatous lesion.

Mr. Trumble also presented a patient with thrombosed hæmorrhoids. He had treated the condition with diathermy. There had been scarcely any pain after the operation and no evidence of infection had been detected. Mr. Trumble pointed out that this was characteristic of the immediate post-operative course when diathermy was employed. So far he had not encountered secondary hæmorrhage. The scar formation was usually trivial.

Public Health.

HEALTH ORGANIZATION.

The League of Nations is unlike any other organization in the world in that, having been established for the purpose of promoting peaceful relations between the nations, it is not restricted by constitutional laws, regulations or rules. It is free to inaugurate and develope any activity which may further its objective. Its members realized from the first that peace depends primarily on national prosperity. Factors which disturb peoples, are therefore those which lead to unemployment, to ill health and high death rates, to unsatisfactory industrial production and to internal and external misunderstandings. Among the various activities that have been called into being by the League of Nations for the purpose of assaying the conditions obtaining in regard to these factors in various countries, mention may be made of the International Labour Office and the Health Organization. Both of these departments deal with matters appertaining to hygiene and the public health. It is proposed on another occasion to publish a short account of the history and development of the Health Organization. For the present we desire merely to call attention to some of the publications of this body. In 1923 the Health Organization started a series of reports on the public health service of the principal nations. Three volumes were published, those of Germany, the Netherlands and Australia. Since then another has appeared from Denmark. In addition four statistical handbooks have been compiled from England and Wales, from Belgium, from the Netherlands and from Spain. All these volumes contain a mass of information which must prove of great value to all other nations in their endeavour to combat disease and avoidable death. In the following some of the more important facts are given from the volume by Dr. Gottfried Frey, of the *Reichsgesundheitsamt* of Berlin.

Public Health Control in Germany.

The Germany *Reich* or realm comprises eighteen federated States. The individual States possess the right to

enact their own laws, but the *Reichstag* or federal parliament has superior powers and can exercise authority over the State legislative bodies. The control of the public health is vested in a federal body called the *Reichsgesundheitsamt* or Imperial Health Board. Certain functions are delegated to the States or to the local authorities, but the general principles on which the control is based, are prescribed by the central body.

The Control of Infective Diseases.

The *Reichstag* has enacted that leprosy, cholera, yellow fever, plague and variola are notifiable. Additions to this list can be made from time to time. The individual States have adopted laws requiring the attending medical practitioner, the head of the household, anyone in charge of the patient, the owner of the dwelling or the coroner to notify the police within twenty-four hours of the fact that someone is suffering from a notifiable disease. The law throws the burden of notification on the medical practitioner; the others are required to carry out the notification only in the absence of a medical practitioner. The diseases that are notifiable in the several States, include diphtheria, cerebrospinal meningitis, puerperal fever, trachoma, relapsing fever, dysentery, enteric fever, glanders, rabies, trichinosis, pulmonary and laryngeal tuberculosis, meat and fish poisoning. In certain States parotitis, morbilli, varicella, pertussis and anchylostomiasis are notifiable, but not in others. Dr. Frey states that a federal bill was being drafted to remove the want of uniformity in this connexion.

The notifications are sent by the doctor on cards supplied gratis for the purpose in an unstamped envelope to the police. The police have to forward the original cards to the medical officer of health of the province, district or municipality. Under certain circumstances medical practitioners are required to communicate with the medical officer of health by telephone or telegraph when an outbreak of an infective disease has occurred. The notifications are forwarded once a week by the medical officer of health to the president of the provincial authority who sends a copy to the Minister for Public Welfare. A further copy is sent to the *Reichsgesundheitsamt*.

Medical officers of health are required to make inquiries in the event of an outbreak of one of the so-called dangerous infective diseases (cholera, plague, variola or yellow fever) in order to trace the origin of the infection. Certain local authorities have the power to institute inquiries in regard to any infective disease or in regard to any death. The medical officers of health may examine any patient or dead body and may carry out any analyses they deem necessary to determine the nature of an infection. In Prussia bacteriological examinations are required immediately the suspicion of cholera, plague, leprosy or typhus (the word in the report is typhus; it should probably be typhoid) fever is aroused. In the presence of an epidemic disease the competent authority may order a *post mortem* examination of all bodies before burial. The regulations governing the compulsory investigation of epidemic outbreaks of infective diseases are somewhat elaborate, but wide powers are given to the central and local authorities, so that the prescribed measures may be applied at the discretion of these authorities. In connexion with some diseases, such as enteric fever, an expert bacteriologist may be sent from the department to carry out the necessary investigations. In the event of an outbreak of a disease which is ordinarily not notifiable in the particular district, special investigations may be carried out with the consent of the police. In such circumstances the result of the investigations must be communicated to the police whose duty it is to forward the information to the appropriate authorities.

Registration of Births and Deaths.

All births must be registered within one week by the legitimate father, the midwife, the doctor or other person present at the birth or the mother as soon as she is fit. Stillbirths or deaths of infants during the birth must be registered not later than the day (week day) following the birth. The birth of fœtuses if the pregnancy has lasted six months or if the duration of the pregnancy is unknown, has also to be notified. Deaths must be registered not later than the day following. The head of the household usually registers the death and consequently the causes of death entered are often inaccurate. It is strange to learn that in certain districts *post mortem* examinations may be and are performed by lay persons, including bath attendants.

Hygienic Arrangements.

The *Reich* or federal authority has undisputed control over all matters affecting the welfare of the population, the care of mothers, of nurslings, of children and of the young, the health of the community and veterinary practice *inter alia*. The *Reichsgesundheitsamt* comprises four departments: a medical, a biochemical, a bacteriological and a veterinary. It is governed by a council which appoints eleven committees to deal with health matters in general, the control of foodstuffs, the prevention of epidemics, the control of water supplies, social hygiene including school hygiene, industrial hygiene, marine and tropical hygiene, communal and racial hygiene, the supply of drugs and the control of poisons, veterinary matters and statistics. In the several States the Ministry for Public Welfare is the public health authority. The health work is administered and controlled by a medical practitioner. Each *Kreis* (large health district) has a full-time or part-time medical officer of health. In Prussia there are four hundred and forty-nine, of whom two hundred and seventy-four are whole-time officers. The *Medizinalräte*, *Regierungsräte* and *Ministerialräte* are medical officers in charge of provinces and groups of districts and in the State central office. The whole organization is a complex one and special training and experience are demanded of candidates for these positions.

Special chapters are devoted to the subjects of the control of hospitals, mental hospitals, lying-in establishments and sanatoria, of the campaign directed against infective diseases, particularly tuberculosis, venereal disease and dangerous infective diseases, of the protection of mothers and infants, of school hygiene and of the campaign against alcoholism. It is impossible to give the details concerning these services in the small amount of space available. If opportunities arise reference may be made to some of these details when we are dealing specifically with the individual subjects enumerated.

Correspondence.

ESSAY ON MATERNAL MORBIDITY AND MORTALITY.

Sir: In reply to the letter of Dr. A. M. Davidson in your issue of September 26, I admit that the available statistics apparently justify his interpretation.

I contend that they also justify mine; in fact I will go further and submit that my interpretation has more justification than his.

We do not know the number of births which occur in the metropolis and which in the ordinary course of events would have occurred in other districts.

We do know, however, the number of deaths of mothers who have come to the metropolis for their confinement. Of these at least 50% come from districts just outside the area which is taken for statistical purposes as the metropolis.

Of those who come from places more distant, about 30% are single women.

The Acting Government Statistician informs me that of the 1,339 metropolitan deaths of women from puerperal causes during the years 1915-24 one hundred and ten were of women from outside the metropolis. In other words the average number of maternal deaths which are incorrectly ascribed to the metropolis is eleven *per annum*.

Transferring these deaths without rectifying the corresponding births (thereby placing the metropolis at a considerable advantage) the metropolitan rate would be reduced from 6.34‰ to 5.82‰ births and that for the remainder of the State increased from 4.89‰ to 5.24‰.

It will be seen that even when "the remainder of the State" is intentionally overloaded, it still shows a lower rate than the metropolis.

If Dr. Davidson contends that all or even the majority of confinements which come to the metropolis from outside districts, are abnormal and that the recorded deaths are to that extent inevitable, he is making a claim for which there is very little evidence. In view of the facts mentioned it seems to me that I have taken a reasonable view of the position and am justified in asserting that "the parturient woman is most safe when furthest removed from centres of population in spite of the better equipment and opportunity for skilled care and treatment found in the latter."

Yours etc.,

E. SYDNEY MORRIS.

93, Macquarie Street, Sydney.
October 1, 1925.

THE CAUTERY IN CHRONIC GONORRHŒA.

THE article of Drs. Gibson and Wylie on the standard of cure in gonorrhœa I quite agree with. A cure really means that there must be an entire absence of signs of inflammation in the urethra and adnexa.

About the utility of the actual cautery there is no argument; in fact it is indispensable in the cure of gonorrhœa, particularly in chronic cases. Personally I never treat any case without it. But with their explanation of its action I entirely disagree. They state that after cauterization of the orifice of the duct of the gland cicatrization occurs which shuts off the gland from the urethra. In the first place it is hard to imagine that cauterization would cause such cicatrization, that it would close a gland that is secreting fluid, let alone one forming pus. In the second place, granted that such a thing could occur, a cyst would necessarily form in some cases which would enlarge until the glandular tissue atrophied.

Cauterization is useless unless it is performed boldly and the whole gland itself completely cauterized. After light cauterization there is left a dimpled cicatrix at the bottom of which is seen the new orifice of the duct. After medium cauterization when the gland has been exposed but only the superficial part destroyed, there is left the dimpled cicatrix with a red, velvety surface formed by the glandular tissue.

Sometimes the glands contain three or four minims of pus, particularly in cases of years' standing, when the glands enlarge to an enormous size and become so superficial that there is no duct to cauterize.

Cysts often form in cases which have received practically no instrumentation. Sometimes in these cases where for weeks daily examination of a smear has revealed no gonococci, they are found after cauterization. This is explained by the fact that the cautery has merely opened into one or more glands without destroying them and gonococci escape into the urethra. These gonococci will persist until the gland is completely destroyed.

Very often on the first cauterization the gland is missed entirely, as the orifice of the duct opens into the urethra some distance from the gland. In these cases the discharge can be seen coming from a certain point after the burn has cleaned up. The cautery must be plunged in this direction. In one of my cases the orifice was over an inch from the gland and to make matters worse the course of the duct was tortuous. It took some months to follow up and ultimately cauterize the gland itself. Gonococci were present until this had been achieved.

Yours, etc.,

W. ERNEST GRIGOR.

207, Macquarie Street, Sydney,
October 10, 1925.

MINER'S PHTHISIS.

SIR: It is generally accepted that this disease is caused by the irritation produced by minute particles of rock which enter the lung. In my youth it puzzled me that some men would contract the disease after very few years underground and others could work a lifetime in the same mines scatheless. There are factors such as constitution to be considered, but observation extending over a quarter of a century has convinced me that there is practically one—does a man use his nose when at work? Most men are nose breathers at rest; few men are nose breathers during exertion. Observe the photographs of men racing, playing football *et cetera*, the mouth open every time. A man should only be allowed to work underground if he can sprint a hundred yards and keep his mouth shut. This simple test in my opinion would do more than all the proposed X raying *et cetera*, which is like bolting the stable door when the horse is dead.

Yours, etc.,

C. JOYCE.

Kelmscott, Western Australia,
September 25, 1925.

Post-Graduate Work.

AN INTERNATIONAL COURSE IN BERLIN.

WE have received a brief notice from the managers of the International Post-Graduate Courses in Berlin concerning a course to be held in October of this year. The notice has been drafted by someone unfamiliar with the English language. It appears that the course has been organized under the auspices of the Faculty of Medicine of the University of Berlin. The course will consist of special lectures in all branches of medical study. Particular emphasis is laid on those subjects which are attracting the attention of the medical profession at the present time. There will be facilities provided for practical work in connexion with these lectures. In the second place lectures on various subjects in medicine proper will be delivered. The lecturers will demonstrate the importance of the specialist in assisting the general practitioner to arrive at a correct diagnosis and to prescribe the correct treatment in affections which present difficulties in either or both directions. The third part of the course will be devoted to systematic lectures on the progress of medical science and technique. Lastly there will be a special course for ophthalmic surgeons. Further details and a complete programme of the course can be obtained by application to the Secretary, Kaiserin Friedrich-Haus für das ärtzliche Fortbildungswesen, Luisenplatz 2-4, Berlin N W 6.

It is regrettable that the organizers of the courses of post-graduate study in Vienna, Paris and Berlin should fall into the unfortunate but unnecessary error of neglecting to recognize that these notices should reach us many months in advance if they are to serve any good purpose. It would be wise if the notices addressed to the profession in the British Empire were submitted to an Englishman for revision or failing this if they were left in the original language. It is not confidence inspiring to read of "Special courses on all medical branch disciplines" in a notice of an international undertaking. The word "discipline" is probably a literal translation of a German word "*Erziehung*" which also means training or education.

Obituary.

JAMES ALEXANDER GREER HAMILTON.

IT is with great regret that we have to announce the death of Dr. James Alexander Greer Hamilton, of Adelaide.

DAVID FRASER LAIDLAW.

WE learn with regret of the death of Dr. David Fraser Laidlaw, of Hamilton, Victoria.

Books Received.

A MANUAL OF PHARMACOLOGY, by Walter E. Dixon, M.A., M.D., B.S., B.Sc., D.P.H., F.R.S.. 1925. London: Edward Arnold & Company. Royal 8vo., pp. xi. + 478. Price: 18s. net.

AIDS TO SURGICAL DIAGNOSIS, by Cecil P. G. Wakeley, F.R.C.S.. 1925. London: Baillière, Tindall & Cox. Foolscap 8vo., pp. vi. + 170. Price: 3s. 6d. net.

ALLERGY, ASTHMA, HAY FEVER, URTICARIA AND ALLIED MANIFESTATIONS OF REACTION, by William W. Duke, Ph.B., M.D., 1925. St. Louis: The C. V. Mosby Company. Royal 8vo., pp. 339. Price: $5.50.

AN INDEX OF TREATMENT, by various writers. Edited by Robert Hutchison, M.D., F.R.C.P. and James Sherren, C.B.E., F.R.C.S.; Ninth Edition, Revised and Enlarged. 1925. London: John Wright & Sons Limited. Royal 8vo., pp. 1035. Price: 42s. net.

BLUE AND OTHER VERSE, by Charles Edgbaston, 1924. London: Heath Cranton Limited. Crown 8vo., pp. vii. + 56.

EYE, EAR, NOSE AND THROAT MANUAL FOR NURSES, by Roy H. Parkinson, M.D.. 1925. St. Louis: The C. V. Mosby Company. Crown 8vo., pp. 207. Price: $2.25.

GYNECOLOGIC UROLOGY, by Lynn Lyle Fulkerson, A.B., M.D., F.A.C.S.. 1925. Philadelphia: P. Blakiston's Son & Company. Royal 8vo., pp. xiv. + 247, with 166 illustrations.

HÆMOPTYSIS IN PULMONARY TUBERCULOSIS, by Dr. Marc Jaquerod, translated by S. F. Silberbauer, M.D., F.R.C.P. (Edin.). 1925. London: Baillière, Tindall & Cox. Crown 8vo., pp. vii. + 106. Price 5s. net.

OCULAR THERAPEUTICS, A MANUAL FOR THE STUDENT AND THE PRACTITIONER, by Doctor Ernst Franke, translated by Clarence Loeb, A.M., M.D.. 1925, St. Louis: The C. V. Mosby Company. Royal 8vo., pp. 183. Price: $3.50.

THE EXTRA PHARMACOPŒIA OF MARTINDALE AND WESTCOTT; Revised by W. Harrison Martindale, Ph.D., Ph.Ch., F.C.S. and W. Wynn Westcott, M.B. (London), D.P.H.; Eighteenth Edition. Volume II.; 1925. London: H. K. Lewis & Company, Limited. Foolscap 8vo., pp. 770. Price: 20s. net.

THE UNIVERSITY OF SYDNEY, ITS HISTORY AND PROGRESS, by Robert A. Dallen. 1925. Second (Revised) Edition. Sydney: The Sydney and Melbourne Publishing Company Limited. Crown 4to., pp. 59. Price: 5s.

Proceedings of the Australian Medical Boards.

QUEENSLAND.

The undermentioned have been registered, under the provisions of *The Medical Act* of 1867, as duly qualified medical practitioners:

Burton, Ernest Joseph, M.B., B.S,. 1924 (Univ. Melbourne), Brisbane.

Grieve, Percy Neil, M.B., 1915 (Univ. Sydney), Winton.

Medical Appointments.

Dr. Reid Innes Campbell (B.M.A.), has been appointed Government Medical Officer at Gatton, Queensland.

* * * *

Dr. David Duncan Cade (B.M.A.) has been appointed Medical Superintendent of the Hospital for the Insane at Mont Park, Victoria.

* * * *

Dr. Richard Buntine (B.M.A.), has been appointed Public Vaccinator at Hughesdale, Victoria.

Medical Appointments Vacant, etc.

For announcements of medical appointments vacant, assistants. *locum tenencies* sought, etc., see "Advertiser," page xvi

JANEFIELD CONSUMPTIVE SANATORIUM, VICTORIA: Resident Medical Officer.

VICTORIAN EYE AND EAR HOSPITAL, MELBOURNE: Three Resident Surgeons.

WINTON HOSPITAL, QUEENSLAND: Medical Officer.

Medical Appointments: Important Notice.

MEDICAL practitioners are requested not to apply for any appointment referred to in the following table, without having first communicated with the Honorary Secretary of the Branch named in the first column, or with the Medical Secretary of the British Medical Association, 429, Strand, London, W.C.

BRANCH.	APPOINTMENTS.
NEW SOUTH WALES: Honorary Secretary, 30 - 34, Elizabeth Street, Sydney.	Australian Natives' Association. Ashfield and District Friendly Societies' Dispensary. Balmain United Friendly Societies' Dispensary. Friendly Society Lodges at Casino. Leichhardt and Petersham Dispensary. Manchester United Oddfellows' Medical Institute, Elizabeth Street, Sydney. Marrickville United Friendly Societies' Dispensary. North Sydney United Friendly Societies. People's Prudential Benefit Society. Phœnix Mutual Provident Society.
VICTORIAN: Honorary Secretary, Medical Society Hall, East Melbourne.	All Institutes or Medical Dispensaries. Australian Prudential Association Proprietary, Limited. Mutual National Provident Club. National Provident Association.
QUEENSLAND: Honorary Secretary, B.M.A. Building, Adelaide Street, Brisbane.	Brisbane United Friendly Society Institute. Stannary Hills Hospital.
SOUTH AUSTRALIAN: Honorary Secretary, 12, North Terrace, Adelaide.	Contract Practice Appointments at Renmark. Contract Practice Appointments in South Australia.
WESTERN AUSTRALIAN: Honorary Secretary, Saint George's Terrace, Perth.	All Contract Practice Appointments in Western Australia.
NEW ZEALAND (WELLINGTON DIVISION): Honorary Secretary, Wellington.	Friendly Society Lodges, Wellington, New Zealand.

Diary for the Month.

OCT. 19.—New South Wales Branch, B.M.A.: Organization and Science Committee.
OCT. 20.—Tasmanian Branch, B.M.A.: Council.
OCT. 20.—New South Wales Branch, B.M.A.: Executive and Finance Committee.
OCT. 21.—Western Australian Branch, B.M.A.: Branch.
OCT. 22.—Victorian Branch, B.M.A.: Council.
OCT. 23.—Queensland Branch, B.M.A.: Council.
OCT. 27.—New South Wales Branch, B.M.A.: Medical Politics Committee.
OCT. 29.—New South Wales Branch, B.M.A.: Branch (Ordinary).
OCT. 29.—South Australian Branch, B.M.A.: Branch.
OCT. 29.—Victorian Branch, B.M.A.: Council, Nomination Paper Issued.
OCT. 30.—Eastern Suburbs Medical Association, New South Wales.
NOV. 3.—Tasmanian Branch, B.M.A.: Council.
NOV. 6.—Queensland Branch, B.M.A.: Branch.
NOV. 10.—Tasmanian Branch, B.M.A.: Branch.
NOV. 10.—New South Wales Branch, B.M.A.: Ethics Committee.
NOV. 11.—Victorian Branch, B.M.A.: Branch; last date of nominations for Council. Election of Scrutineers.
NOV. 11.—Victorian Branch, B.M.A.: Clinical Meeting Children's Hospital.

Editorial Notices.

MANUSCRIPTS forwarded to the office of this journal cannot under any circumstances be returned. Original articles forwarded for publication are understood to be offered to THE MEDICAL JOURNAL OF AUSTRALIA alone, unless the contrary be stated.

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